INTRAMUSCULAR INJECTIONS OF OLEUM CINEREUM in the TREATMENT OF LUES

with

RESEARCHES AS TO

the Absorption and Elimination of

MERCURY

and its action on

THE SPIROCHAETA PALLIDA

and

CLINICAL EXPERIENCES OF THE METHOD.

A THESIS FOR THE DEGREE OF M.D. PRESENTED IN 1908.

by

ROBERT WILLIAM MACKENNA, M.A. 1896. M.B.Ch.B. 1898.

123, Hartington Road,
Sefton Park,
Liverpool.

INDEX

PREFACE

This Thesis may be divided into two parts, the former of which embodies a considerable amount of personal research, while the latter is taken up more particularly with Clinical Experiences.

The greater part of the original observations will be found in Chapters, II., III., IV.

The work on which this Thesis is founded has been done almost entirely in the Liverpool Skin Hospital: and I am much indebted to the Senior Physician, Dr. Stopford Taylor for his kindness in placing at my disposal all the resources of his Clinique.

CHAPTER

I

INTRODUCTORY.

CHAPTER

1

Introductory.

CONTENTS:- Mercury in Syphilis:-
Intramuscular Injections:-
Choice of Preparation:-
Grey Oil:- Site,
Technique and Frequency of Injections:-
General Rules:-

--o0o@o0o--

Mercury has long been recognised as the most potent remedy for Syphilis. Since its efficacy was first discovered there has been a constant search for a method of administration which would ensure its fullest therapeutic effect and expose the patient to the least risk of Mercurial poisoning. Administration by the mouth, inunction, and fumigation were, for many years, the only methods for its exhibition. Each of these methods is excellent, but all have this serious disadvantage that it is impossible to measure accurately the precise amount of mercury absorbed by the patient. Much of the mercury given by the mouth passes unabsorbed out through the intestine. It provokes

Peristalsis, and hastens its own passage through the bowel, so that when we administer, e.g. nine grains of Hydrargyrum cum Cretâ daily to a patient, we do not know the exact dose of mercury which he will absorb. In the same way we have no clue to the amount of mercury which a patient absorbs at each rubbing, while fumigation is the most inaccurate method of all. Treatment by intramuscular injections of mercury, which was first suggested by Hunter and Hebra and brought into fame by Scarenzio, fulfils this great requisition of scientific treatment, viz. accuracy of dosage, for before the drug can be eliminated from the system the whole amount injected must be absorbed and pass through the lymphatic and blood circulation. One sixth of a grain of Calomel, for example, or a grain of Metallic Mercury injected into the gluteal muscles cannot escape from the system, without being wholly absorbed. To this statement there is one exception possible: viz. the formation of an abscess at the site of injection, and the consequent escape of the mercury with the abscess contents. But, as I have personally administered close on ten thousand intramuscular injections of mercury, and have never seen an abscess produced by it, I think this possible means of escape for the Mercury is negligible.

At the present day the treatment of Syphilis by intramuscular injections is practised, to the almost total exclusion of any other method, in Germany, Austria, Belgium and France. At Aachen and Wiesbaden inunction is still the favourite method, but there too the intramuscular method is occasionally employed. In our Army, thanks in great measure to the work of Lambkin, the intramuscular method is the method of choice, and to-day it is regaining in many hospitals and with many Medical men, the popularity which it had previously acquired, until, through faulty technique and inaccurate methods, it fell into an unmerited disrepute.

The following Thesis is the fruit of my experience of this method during the past four years. In the course of my work I have prosecuted some research into the rate of absorption and elimination of Mercury injected intramuscularly, and the conditions which affect these processes. I have also investigated the action of Mercury on the specific organism of Syphilis - the Spirochaeta Pallida, or, as it is now usually designated, the Treponema Pallidum. I have further investigated the frequency with which the Spirochaeta Pallida is met with in Syphilitic lesions, and have studied the characters of the organism as met with

in microscopical preparations derived from syphilitic patients. These researches together with my clinical experience of the method are embodied in the following pages.

CHOICE OF PREPARATION:-

For the intramuscular injection of Mercury one has choice of two varieties of Mercurial preparations, viz.

(a) Soluble Salts.
(b) Insoluble Salts.

Of the former class, which is quickly absorbed, and quickly eliminated, the usual types are the Perchloride, Biniodide, Benzoate, Lactate, and Sozo-iodolate of Mercury, and also Hermophenyl- a compound of Oxide of Mercury and Phenol bisulphite of soda. These preparations, because of their rapid absorption and consequent speedy passage from the system, must be administered at short intervals - twice or thrice weekly, or even more frequently.

Of the insoluble salts the chief used are Calomel, which is undoubtedly the most active, basic salicylate of Mercury, which is at present being largely used in Germany, Mercuric Oxide, Green Iodide of Mercury and Metallic Mercury, in the form of Oleum Cinereum, or Grey oil.

GREY OIL:-

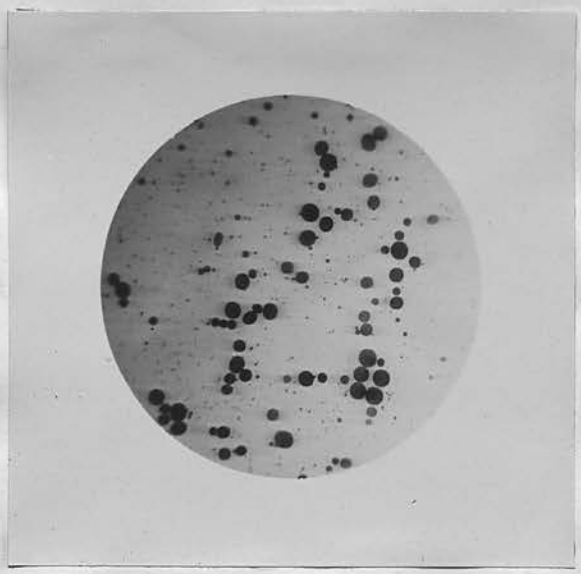
It is this last preparation, viz. Grey Oil which I have chiefly used, though, in a few cases, I have had recourse to injections of Calomel and Sozo-iodolate of Mercury.

The formula-"Lafay's"-for Grey Oil is as follows:-

℞.

Purified Mercury	40 grammes.
Sterilised anhydrous Lanoline	12 "
Sterilised white Vaseline	13 "
Sterilised Medicinal Oil of Vaseline.	35 "
	(all by weight)

The oil contains 40% by weight of metallic Mercury, and forms a fairly thick, slate-coloured cream.



MICROPHOTOGRAPH OF GREY OIL X 450 DIAMETERS.

In its preparation scrupulous care should be taken to ensure sterility.

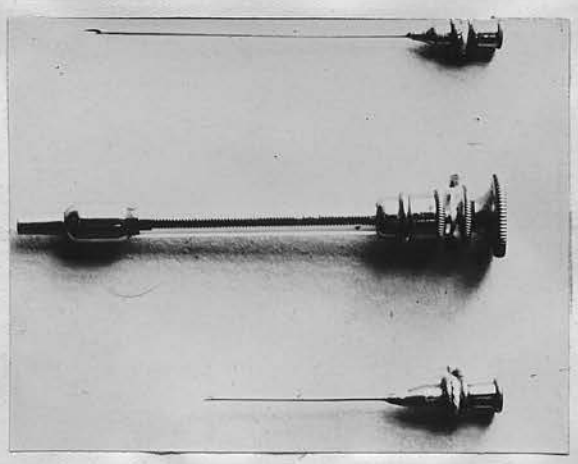
Before use it should be thoroughly stirred with a sterilised glass rod, and, in cold weather, when it tends to become too thick, it should be

gently warmed before stirring.

For administering the oil it is well to use a syringe graduated in such a manner that each division corresponds to a definite weight of metallic Mercury in the oil.

I have used Barthélemy's syringe exclusively when injecting Grey oil. It is graduated so that each division, of which there are fourteen, corresponds to an amount of oil containing one centigramme of Metallic Mercury. Platino-iridium needles, which resist the corrosive action of the Mercury, should always be used. They can readily be sterilised, either by heating in the flame of a spirit lamp, or, as is done at the Military Hospital, Rochester Row, London, they may be dipped for a moment in boiling oil! The needles should be of sufficiently wide bore to allow the easy passage of the oil through them; and should be of two sizes: viz. 5 C.M. long for thin adults, and 7 C.M. for well-nourished patients with a thick layer of fat between the skin and the subjacent gluteal muscles.

BARTHELEMY'S SYRINGE



DOSAGE:-

A suitable dose for an adult man weighing from ten to twelve stones is eight centigrammes of Mercury per week. In urgent cases, or in men weighing more than twelve stones it is a good thing to begin treatment with a dose of twelve to fourteen centigrammes, decreasing subsequent doses to six or seven centigrammes weekly. Women, unless they are of massive build and strong physique should be given the smaller dose- viz. seven centigrammes from the first, unless there is some indication for more active treatment.

SITE OF INJECTION:-

Many areas, more or less complicated to define, have been marked out on the buttocks by various observers, as offering the only safe regions for these injections.

Wickham (1) recommends a circle about two inches in diameter, whose centre is at the intersection of two lines one of which passes through the junction of the upper $\frac{1}{4}$ and the lower $\frac{3}{4}$ of the buttock, while the other divides the internal $\frac{1}{3}$ from the external $\frac{2}{3}$ of the same region. These measurements are too elaborate for everyday use, and safer areas of the buttock can be found with less waste of time.

Grosz (2) marked out a triangle the corners of which are situated:-

(a) Midway between the great Trochanter and the Tuberosity of the Ischium.

(b) A point midway between "a" and a horizontal line drawn across the back at the level of the Anterior Superior Iliac spine, and:-

(c) A point on the same level as "b" and midway between the Great Trochanter and the Anal fissure.

Galliot has recommended the spot where a horizontal line drawn two fingers' breadth above the Great Trochanter, is cut by a vertical line drawn two fingers' breadth distant from, but parallel to the Intergluteal furrow.

Smirnoff's point is more easily defined, and lies two fingers' breadth above and internal to the Great Trochanter. I have occasionally, as will be seen in the next chapter, made use of this area, but, as a rule have found that Barthélemy's area, viz. the middle of a line drawn between the Anterior Superior Iliac spine, and the upper end of the Inter-gluteal furrow, is the most suitable. Here the danger of wounding vessels or nerves is reduced to a minimum, while there is an adequate thickness of muscle, and the injection is not likely to interfere either with sitting or riding.

ATTITUDE OF PATIENT:-

If a man, the patient should stand with his buttocks exposed to a good light, and with his back to the administrator. If the injection is to be given on the right side, the patient should

stand firmly on the left foot, and relax the muscles of the right buttock by raising his right heel from the ground, and slightly flexing his knee. If the patient is a woman, the injection may be made while she lies prone.

TECHNIQUE:-

Having made out one's landmarks the skin should be rubbed briskly with a pledget of wool soaked in methylated spirits, which, in my experience, is the best antiseptic for the purpose.

The syringe having been filled with the dose one intends to administer, the needle should be detached, and held firmly between the finger and thumb, and thrust deeply with a sharp plunge into the muscle under the disinfected skin. If this is done quickly there is no pain beyond a sudden prick as the needle passes through the skin. Thirty or forty seconds should be allowed to elapse before the loaded syringe is fitted to the needle, and the injection administered, to make sure that the needle has not penetrated any blood vessel. In the event of any blood escaping from the needle, which indicates that it has struck a vessel, it should be withdrawn, and inserted again elsewhere. To make quite sure that the needle has not penetrated a blood-vessel one may fit to it, as it lies in the tissues, an

empty syringe and exhaust it, a proceeding which will at once draw blood into the barrel, if a vessel has been pierced. When one is satisfied that the needle is not in a danger zone, the loaded syringe should be adjusted carefully to the butt of the needle, and its contents driven into the muscles with a slow and steady pressure. When the syringe is empty it should be withdrawn quickly, with the needle, in one piece, and the point of its entrance should be massaged vigorously for half a minute to facilitate the distribution of the Grey Oil between the muscle fibres. No dressing is required. The operation, if performed carefully and quickly, is painless, and as Grey Oil is not an irritating preparation there is little subsequent discomfort. From forty-eight to sixty hours after an injection, the patient may sometimes feel a slight stiffness at the point of injection, which is not, however, sufficiently marked to interfere with his comfort or his work. I have administered injections to Cavalry-men, Tram-drivers, who control a heavy brake with their feet, artisans of all kinds, laundry women, cyclists, and a professional acrobat, in all of whom it was essential that there should be no interference with the power of their limbs, and in none of them was the resulting discomfort sufficient to interfere with their full activity. Most patients are quite unaware of any discomfort whatever, and I have only known of one man who complained of actual pain after each injection. The reason for this could not be ascertained:

and, singularly, when the injections of Grey Oil were suspended, and injections of Sozoiodolate of Mercury made into his deltoid muscles, he made no further complaint.

FREQUENCY OF INJECTIONS:-

The injections should be made weekly into alternate buttocks, the amount of Mercury, and the total number of injections being controlled by the physique of the patient, the progress of the disease, and the rate at which the Mercury is being eliminated by the urine. These points will be discussed in greater detail in a subsequent chapter. Meantime it will suffice to say that the immediate manifestations of the disease are well under control after six weekly injections of seven Centigrammes of Grey Oil, and the dose of Mercury may be lessened, or given fortnightly instead of weekly till in all ten or twelve injections have been administered.

No disease can be treated on hard and fast lines, and the amount of Mercury administered must be regulated by many considerations. My experience has not shown that any real advantage is to be derived from "intensive" methods of treatment, such as Duhot (3) advocates, in which the patient is loaded up with enormous doses of Grey Oil given at short intervals. Disaster lies that way, and discredit falls on the method.

In fresh cases of syphilis, one should aim at giving at least three courses of injections during the first twelve months, spread over the year as follows:-

FIRST COURSE:- Six to twelve injections of seven centigrammes each, spread over three months, and followed by an interval of two months.

SECOND COURSE:- Six to eight injections of seven centigrammes, spread over three months and followed by an interval of two months.

THIRD COURSE:- Four injections of seven centigrammes, spread over two months.

This gives as a maximum for three courses:- subject to variation as occasion may require:- twenty-four injections in the course of a year:- and as an absolute minimum, below which one should rarely, if ever, go:- sixteen injections.

If the type of disease is very severe four courses may be given in the year:- the second course being spread over only two months, the third over four weeks, and the fourth, of four weekly injections, after an interval of a month from the termination of the third course.

As will be shown in chapter 3 such a method of intermittent treatment keeps the system constantly under the influence of Mercury.

In the second year, three short courses comprising in all eighteen injections, or two longer courses making the same total should be administered as follows:-

Second Year's Treatment:- which should begin not longer than three months after the termination of the first year's final course.

FIRST COURSE:-

Nine to twelve injections of seven centigrammes, spread over three months, followed by an interval of three months.

SECOND COURSE:-

Six to nine injections of seven centigrammes spread over three months,

Or:-

FIRST COURSE:-

Nine injections spread over three months followed by an interval of six weeks.

SECOND COURSE:-

Six injections spread over two months followed by an interval of six weeks.

THIRD COURSE:-

Three injections spread over one month.

In the third year, twelve injections should be given:- in two courses of six:- with an interval of three months between them.

GENERAL RULES:- Certain general rules should be carefully observed during treatment with Grey Oil.

The teeth should be carefully examined before each course, and those hopelessly decayed should be removed by the dentist, while those that can be saved should be filled. Scrupulous cleanliness of the buccal cavity should be insisted upon, and the patient should be told to brush the teeth after each meal, and rinse out the mouth thoroughly with an antiseptic or astringent mouth wash. I have found the following suit admirably:-

℞.

Potassii Chloratis	drachms III
Sod. Biboratis	drachms III
Tinct. Opii Aquosae	drachms VI
Aq. Menth. Piperitae ad	oz VIII

Sig. To be diluted with an equal quantity of water and used after each meal.

Even hospital patients learn the importance of keeping the teeth clean, if a careful examination of the buccal cavity is made at each visit. The slightest sign of Stomatitis should be an indication to cease from administering Mercury, and the gums can soon be restored to a healthy condition by applying a solution of silver nitrate containing one drachm per ounce, to the affected parts. In private practice I have only seen one case of Stomatitis arising from Mercurial injections, and it was not severe, and in hospital practice, among close on six hundred patients with Syphilis, less than six cases, all of which were slight and four

of which were in intemperate patients, who would not attend to instructions.

Each patient should be weighed before each course of Intramuscular treatment commences, as well as frequently during the course: and any falling off in weight should be counteracted by ordering an increased diet. The dose of Mercury should also be lessened.

The urine should be examined, especially for albumen, and this examination should be repeated from time to time during treatment. The presence of albumen is not an absolute contra-indication to treatment by injection, but, if found, its cause should be investigated, to ascertain whether it is due to a pre-existing Nephritis, or is a Syphilitic Albuminuria. If the former is the cause, treatment with Grey Oil is contra-indicated. If the albuminuria is a syphilitic manifestation treatment should commence very gradually, with doses of two or three centigrammes weekly, and the albumen should be estimated quantitatively from day to day. If due to Syphilis it will soon show signs of diminishing; but any increase in its amount, should be regarded as a danger signal and an indication to cease intramuscular injections.

During each course, the urine should be examined from time to time for Mercury: and before each successive course, to ascertain if all the

Mercury administered during the previous treatment has been eliminated. The method of doing this, and the results obtained from researches I have made upon this point will be found in Chapter III.

Finally, before treatment is instituted, the seriousness of the disease, the danger of communicating it to the innocent, and the need of prolonged treatment, should be impressed upon the patient. At the same time all stimulants and tobacco should be forbidden, and the patient encouraged to lead a healthy life, free from excesses of dissipation or of work.

CHAPTER

II

THE ABSORPTION OF MERCURY

INJECTED INTRAMUSCULARLY.

CHAPTER

II

The Absorption of Mercury injected Intramuscularly.

CONTENTS:-

---o0@0o---

The rate at which Medicinal substances introduced into the body by any of the available routes are absorbed is necessarily a matter difficult to ascertain. In the case of drugs given by the mouth it is practically impossible to determine the length of time required for their complete absorption. That absorption has commenced may be gathered from the appearance of those symptoms which characterise the action of the drug. If we administer opium to a patient, and he falls into a deep sleep with contracted pupils, we know that the absorption of the opium has begun and is well established. That other drugs are being absorbed we may learn from the appearance of their

therapeutic effects, or by their appearance in the urine. But in the case of Grey Oil administered intramuscularly we have the power of watching and recording its absorption until it has disappeared completely from the site at which it was injected. The "X Rays" are the means which place this power in our hands. Mercury being a metal and denser than bone gives a darker shadow on a photographic plate than osseous tissue does: and it is possible, with a sufficiently strong current, and "X Rays" of sufficient penetration, to secure radiographs which show the mercury lying in the muscles behind the Ilium, or at whatever other point it may have been injected. In taking the radiographs which illustrate this chapter, I have always placed the patient on his or her back, with the buttock to be radiographed lying on a large photographic plate inclosed in a "light-tight" bag. The vacuum-tube has been one of medium hardness, the spark gap has been from 3 - 4 inches: the current in the primary circuit has been 20-25 ampères, and the current driven through the tube has been 2-3 milli-ampères. I have had a valve-tube in circuit: and the "break" has been Wehnelt's electrolytic interrupter. The average duration of exposure has been 20-30 seconds, and the distance between the anticathode and the photographic plate has been twelve inches. Unfortunately with such strong currents as are required for securing a radiograph

of the pelvis, it is impossible to subject any patient daily to their influence, lest the skin over the region skiagraphed should be completely destroyed. But without much danger one may take such radiographs every four or five days, and this is the procedure which I have usually followed. As a rule I have made the injections in patients I intended to radiograph in the usual site- viz. at Barthelèmy's point: but in some cases, in order that the Mercury might be seen clear of the bony shadow, I have made the injection at Smirnoff's point above and behind the great Trochanter.

A word of caution is necessary before one proceeds to study any radiographs of the pelvis. The Röntgen Rays do not give a photograph in the true sense, but simply a shadowgraph: and consequently all contour is lost in the picture, which is flat. In consequence of this flatness it is rather difficult, unless one is accustomed to the examination of radiographs, to judge accurately of relative position: and injections made at Smirnoff's point would seem, according to radiographic evidence, to be in dangerous proximity to the hip-joint: while, as a matter of fact, the injected oil is well away from this point lying in the gluteal muscles above and behind it.

THE DISPOSITION OF MERCURY INJECTED INTRAMUSCULARLY IN THE TISSUES:-

Before proceeding to study the results obtained from the Radiographic examination of patients treated by intramuscular injections it will be of advantage to consider how Mercury disposes itself when injected into the muscles. To clear up this point I have made a series of observations on the cadaver. I have warmed the Grey Oil to body-temperature previously to injecting it, and have then proceeded exactly as in the living subject. After making the injections I have cut down, with as little disturbance of the parts as possible, on the deposit of Mercury. As a rule one finds that the oil is not deposited in a mass or "blob," but has distributed itself in one or more lines of varying breadth between the muscle bundles. It is not the rule to find that the Grey Oil flows back along the needle track, provided the needle is withdrawn quickly, but occasionally this may happen and some of the Mercury is found in a streak following the track of the needle. Massage, if well applied, is of material aid in distributing the Grey Oil, which is found spread out in a thin layer between the muscle fibres if the parts have been massaged for a few minutes after an injection.

THE EVIDENCE OF RADIOGRAPHS:-

If a radiograph is sufficiently good to

show the outline of the bones it will reveal any Mercury that is present. If I have known Mercury to be present in the muscles, I have never failed to be able to see it in the radiographic plate when examined by transillumination, and I think one is justified in concluding from this that if one can see from day to day the gradual diminution of a deposit of Mercury in the tissues, and a point is ultimately reached when the Mercury ceases to be visible, the metal has been completely absorbed.

That this absorption is slow may be seen from an examination of the radiographs on p.p. I—21 of the Portfolio of illustrations which accompanies this Thesis. But the absorption is progressive, a fact that is proved inasmuch as no two successive radiographs taken at an interval of twenty-four hours from each other, show exactly the same features. Either the shadow of the Mercury appears thinner, or the outline is more broken in successive pictures: and absorption continues with a diminution of the intensity of the shadow, and a narrowing of its outlines, most often with accompanying interference with its continuity, so that it presents the appearance of a number of separate deposits, until it completely disappears. The date of its disappearance varies with the individual, but I have always found that the same patient absorbs at approximately the same rate. In some cases 7 centigrammes

of Mercury will have disappeared completely from the muscles in a week or ten days. But this is exceptional: and my experience has been that, as a rule, a dose of seven Centigrammes is not completely absorbed till 14 or sixteen days have elapsed from the time of its injection.

Relatively, the larger doses are absorbed somewhat more quickly. At the end of a week an injection of 14 cgs. will have lost an appreciable proportion of its bulk, and is usually completely absorbed at the end of three weeks, though I have seen, in one case, faint traces of Mercury as long after injection as five weeks.

The most satisfactory way of arriving at an idea of the rate at which Mercury injected intramuscularly is absorbed, will be to examine seriatim the 18 radiographs contained in the Portfolio of illustrations presented with this Thesis.

RADIOGRAPH 1.

This Radiograph was taken on the same day as the patient received an injection of 14 cgs. of Mercury. The deposit of Mercury is seen lying in the muscles above and behind the hip-joint.

RADIOGRAPH 2.

The same patient one week later. There is an obvious diminution in the depth of the shadow thrown by the Mercury.

RADIOGRAPH 3.

This Radiograph shows the same side of the Pelvis a fortnight after Radiograph No.I. The shadow of the Mercury is almost invisible.

RADIOGRAPH 4.

This Radiograph was taken three weeks after No.1. The Mercury injected three weeks previously has completely disappeared.

In this case the rate of absorption was of average rapidity. In the next case the rate of absorption was somewhat slower.

RADIOGRAPH V.

This Radiograph was taken 14 days after the administration of 14 cgs. of Mercury. A considerable amount of Mercury is seen lying in the tissues.

RADIOGRAPH 6.

The same case 4 days after the previous Radiograph. An appreciable diminution of the Mercurial deposit may be noticed.

RADIOGRAPH 7.

The same patient 24 days after the administration of the injection.The Mercury still is present in sufficient quantities to show a faint shadow.

The following Radiographs Nos. 8 and 9. show the difference in the shadow given by the Mercury at an interval of 48 hours in a patient in whom absorption took place at average rate.

RADIOGRAPH 8.

This Radiograph shows an injection of seven Centigrammes lying in the tissues.

RADIOGRAPH (Continued) 8.

It was taken one hour after the administration of the injection., and the Mercury is seen lying in a fairly continuous streak.

RADIOGRAPH 9.

The same patient as No.8. 48 hours later. The streak of Mercury is broken up in several places.

The following two Radiographs show the effect of Massage in distributing the Mercury in the tissues, and also in promoting absorption.

RADIOGRAPH 10.

This shows a deposit of 7 cgs. of Mercury lying in the Gluteal Muscles covering the Ilium. Vigorous Massage was applied for 2 minutes after the injection was administered, and the Radiograph was taken immediately afterwards. The Mercury is lying in a flattened out film between the muscle fibres.

RADIOGRAPH 11.

This Radiograph was taken one week after Radiograph 10 and shows the almost complete absorption of the Mercurial deposit.

RADIOGRAPH 12.

This Radiograph shows a somewhat unusual form of Mercurial deposit. One does not usually see the metal distribute itself in such a definite, unbroken streak.

RADIOGRAPH 13.

An injection of 7 centigrammes of Mercury is seen lying behind the Ilium.

RADIOGRAPH 14.

The same injection as is seen in Radiograph 13, after Massage for two minutes. The Mercury is more distributed through the muscles

RADIOGRAPH 15.

The same patient as Nos. 13 and 14 one week after the injection. In this case also the effect of Massage in promoting absorption is seen, and the deposit of Mercury has completely disappeared.

RADIOGRAPH 16.

This Radiograph shows an injection of seven centigrammes of Mercury lying behind the Ilium. The Radiograph was taken 24 hours after the injection.

RADIOGRAPH 17.

The same deposit as is seen in Radiograph 16 four days later.

RADIOGRAPH 18.

The same patient as Nos. 16 and 17 one week after the injection was administered. The Mercury has almost completely disappeared.

From a study of the Radiographic evidence it is apparent that Mercury administered intramuscularly in the form of Grey Oil is absorbed slowly, But in every case the absorption is progressive, and there is no evidence of what one may call Mercurial stagnation.

However, the evidence goes to prove that intramuscular injections of Grey Oil must not be administered at random without regard to the slow rate at which the Mercury is absorbed. And one must not administer these injections in an indefinite number but cease their administration as soon as the disease is well under control. The necessity of examining the urine to ascertain whether the Mercury is being eliminated satisfactorily, is also brought home to us by the Radio-graphic evidence. With caution there is nothing to be feared from the slow absorption of the Mercury, which is one of the chief qualities to which intramuscular injections of Grey Oil owe their superior efficacy.

CHAPTER

III

THE ELIMINATION OF MERCURY

CHAPTER
III

The Elimination of Mercury in the Urine.

CONTENTS:-

---oO@Oo---

Mercury administered in any way is eliminated in the Secretions and Excreta:- in the Urine, faeces, saliva, sweat, and, in nursing mothers in the milk, and in Pathological Secretions, such as the pus of an abscess or the discharge from an ulcer. The date at which it appears in the Urine, which is one of the chief vehicles for conducting it from the body, depends in the first place upon the nature of the salt and the method by which it is administered. It is reasonable to expect that a soluble

salt, administered intra-venously, will appear in the urine more rapidly than an insoluble preparation given either by the mouth or injected intramuscularly.

Davidescu(4) found that after the intramuscular injection of soluble salts he could discover traces of Mercury in the urine in six to eight hours: while Mercury administered by the mouth was not discoverable in the urine for four or five days.

Lhereux(5) who has employed massive doses of biniodide of Mercury after the method of Prokhorov says that he found the metal in the urine one hour after administering a dose of four centigrammes.

I have examined the urine of a large number of patients with a view to studying the rate of elimination of Mercury, and the following facts are based upon analyses of 150 cases.

THE DETECTION OF MERCURY IN THE URINE.

There are many methods of detecting Mercury in the urine, all of which are slow. The one which I have invariably used is that first described by Stukowenkoff, and is as follows:-

Five Cubic centimetres of a saturated solution of common salt are rubbed up in a mortar with an equal qnantity of white of egg: the Albumen and salt solution is then poured into a beaker, containing 500 cubic centimetres of the urine to be

examined, and gently stirred through it. The beaker is then placed in a water-bath and slowly heated till the albumen is completely coagulated. This usually requires an hour.

The urine is then filtered through filter-paper, and the albumen, with which the Mercury in the urine has combined, is rubbed up in a mortar with ten cubic centimetres of pure hydrochloric acid. It is then placed in a large test tube: several pieces of copper wire are dropped into it, and enough strong hydrochloric acid is poured in to bring the total amount in the tube up to 50 c.c.

The tube is then placed in a cool place for twenty-four hours, by which time the albumen is completely digested and the Mercury has been deposited on the copper. The copper wire is removed, and washed successively in cold water, hot water, methylated spirits, and ether, and then dried in the air. When quite dry the copper is placed in a narrow piece of glass tubing, about six inches in length, closed at one end, and a few crystals of Iodine are dropped on the upper end of the copper. Gentle heat is applied from below upwards which drives the Mercury off the copper in a fine vapour. The Mercury and Iodine combine, and as the heat ascends the tube, are driven up to the cooler portion, where, if the tube be kept rotating, they settle in a red ring of Biniodide of Mercury.

The amount of Mercury can be gauged by the breadth of the red deposit, and a series of rings may be made from definite quantities of Mercury and in this way a useful scale may be prepared for purposes of comparison.

The scale which I have used, I have prepared in the following manner. I have dissolved in 500 c.c. of urine a quantity of Bichloride of Mercury, whose actual Hydrargyrum content was, as near as possible, 40 milligrammes, and proceeded according to Stukowenkoff's method, adding to the urine, however, a somewhat larger quantity:- viz. three drachms each of albumen and saturated salt solution. After coagulation and filtration, I have digested the albumen for twenty-four hours in twenty drachms of strong Hydrochloric acid.

There being therefore, 40 milligrammes of Mercury in twenty drachms of acid, there will be 2mgs. of Mercury in one drachm, and 1 mg, in thirty minims, and .50 mgs. in 15 min: and so on.

Into quantities of the acid containing approximately, .25, .5, .75, 1, 1.25, 1.50, 1.75, 2 and 2.25 milligrammes, I placed small quantities of copper wire, and left them for twenty-four hours. On subliming the Mercury as in Stukowenkoff's method, and combining it with Iodine to form the Biniodide, one got a serviceable scale for comparison,

the depth and thickness of the ring deposited in the tube varying for each amount of Mercury. In comparing the standard scale with other tubes it is difficult to distinguish differences of less than .25 milligramme, so that there is room for that amount of error, but in practice the scale works out satisfactorily.

The following table shows the time when Mercury first appeared in the urine of twenty patients.

N.B.

In this, and in all other tables or analyses in my Thesis dealing with the Elimination of Mercury, unless when otherwise stated, the amount of Urine examined was 500 c.c. from a mixed 24 hour sample. In this way some basis for comparison between the rates of Elimination of Mercury, administered in various ways, can be attained; and if it be urged that Mercury could be discovered in the whole 24 hours urinary output at an earlier date than it could be found in a part of the daily excretion, it must be remembered that, in the same way, it will have become unrecognisable in a 500 c.c. sample before it has disappeared from the whole daily output.

No.	Sex	No.Of Inj:	Amount Injected	Date Of Appearance In Urine Of Mercury.
1.	Male	1	14 cgs.	7 Days after Injection.
2	Male	2	(Each Of) (7 cgs.)	(2 Days after 2nd Inject) (9 days after 1st Inject)
3	Male	1	14 cgs.	6 days after Injection.
4	Male	1	14 cgs.	7 Days after Injection.
5	Male	2	(1 Of 14) (cgs.) (1 Of 7)	8 days after 1st Inject:
6	Female	2	(1 Of 14) (cgs.) (1 Of 7)	10 Days after 1st Inject:
7	Female	1	14 cgs.	7 Days after Injection.
8	Female	2	(7 cgs) (each)	10 Days after 1st Inject:
9	Male	2	(7 cgs.) (each)	9 Days after 1st Inject:
10	Male	2	(7 cgs.) (each)	10 Days after 1st Inject:
11	Male	1	7 cgs.	4 Days after Injection.
12	Female	2	(7 cgs.) (each)	13 Days after 1st Inject:
13	Female	2	(7 cgs) (each)	11 Days after 1st Inject:
14	Female	1	14 cgs.	9 Days after 1st Inject:
15	Male	1	7 cgs.	8 Days after 1st Inject:
16	Male	1	14 cgs.	6 Days after 1st Inject:
17	Female	2	7 cgs.	8 Days after 1st Inject:
18	Female	2	7 cgs.	9 Days after 1st Inject:
19	Male	2	7 cgs.	8 Days after 1st Inject:
20	Male	2	(14 and) (7 cgs)	8 Days after 1st Inject:

The above table deals with twelve male and eight female patients, and it will be seen that the Male patients eliminate Mercury by the kidneys a little more quickly than the female patients, Whereas the average interval elapsing between the administration of a single dose of fourteen Centigrammes, and the appearance of recognisable Mercury in the urine was six and a half days in the male patients, the average interval in female patients was eight. In cases in which two doses of seven Centigrammes were administered before the Mercury was detected, the average time in male patients between the first dose and the discovery of Mercury was $8\frac{4}{5}$ days: and in female patients $10\frac{1}{5}$ days. In cases in which an initial dose of 14 centigrammes was followed by one of 7 centigrammes the following week, the male patients showed an average time for the disappearance of Mercury in the urine of eight days, while the only woman of whose case I have a record who was treated with these doses, required ten days before the Mercury could be found in the urine.

The shortest interval I have known to elapse between the administration of 7 cgs. of Mercury and its discovery in the urine was four days, but as this patient had two treatments of fifteen minutes each on the High Frequency Induction Couch, I believe that the High Frequency current stimulated

his eliminating functions. In one other patient, a man with severe nerve Syphilis, exhibiting partial paresis of the left half of his body I noticed the High Frequency Current had a similar effect. He eliminated Mercury very slowly, but as soon as he began to have High Frequency Treatment he began to eliminate Mercury in larger quantity. The latest date of which I have any record as to the first appearance of Mercury in the urine after two injections of seven centigrammes is thirteen days. The patient was a woman. In these cases in which the appearance of Mercury in the Urine is much delayed, I am inclined to think that elimination begins first through the bowel. Exercise and active Metabolism certainly facilitate the elimination of Mercury, and it is for this reason that as a rule Mercury appears earlier in the urine of male than female patients.

THE CURVE OF ELIMINATION:-

Once the elimination of Mercury by the kidneys has been established it goes on steadily, increasing in amount with each successive injection. The rise in the curve of elimination is almost always progressive and regular, and reaches its height a variable time after the last injection has been administered, Thus, if we systematically examine the urine of a patient who has had a series of six weekly intramuscular injections, we will find that each week there is an increase in the

amount of Mercury he eliminates. This increase, however, continues after the injections cease, and reaches its height at the seventh, eighth, ninth or tenth week. Those patients who began elimination late, reach the zenith of elimination late.

The height of elimination being reached there is usually a period varying in length from two days to a week, during which the elimination is approximately constant. Then the elimination curve begins to fall, falling by lysis rather than by crisis. (See charts 1.& 2 in Portfolio of illustrations. p.p. 22 — 23.)

This is true of most patients, but occasionally, in delicate people with scanty nerve force, elimination is not quite so steady, the patient eliminating more one week than another.

THE EFFECTS OF INTERCURRENT ILLNESS ON ELIMINATION.

Intercurrent illnesses also lessen the elimination as they probably also retard absorption.

CASE:- A young man, aged twenty-four, who was eliminating Mercury steadily, contracted influenza. During the febrile stage, the elimination of Mercury in his urine dropped considerably, falling from three milligrammes daily to less than two milligrammes, but rose again as convalescence was established. I have noted the same fact in the case of a young

man who while under treatment for Syphilis, contracted measles, and also in another patient who developed rheumatism. The simultaneous administration of Potassium Iodide by the mouth, while a patient is having a course of intramuscular injections, also hastens elimination by the kidneys, as well as by the mucous membranes.

CASE 2. A man aged fifty had had six intramuscular injections each of seven centigrammes of Mercury, and was eliminating it satisfactorily, and passing 1.5 milligramme in each 500 c.c. of urine. He was given, in addition, 10 grains of Potassium Iodide thrice daily because of nocturnal headaches. There was a sudden increase in the amount of Mercury he was passing in the urine, and simultaneously he developed slight ptyalism, due I believe to a sudden increase in the amount of Mercury eliminated by the mucous membrane of the mouth. On stopping the Potassium Iodide the amount of Mercury he eliminated decreased, and the ptyalism soon ceased. This observation, made in the early days of my acquaintance with the intramuscular method, I have several times repeated: and if I have ever had occasion to administer Potassium Iodide to a patient who is having injections, I have always been on the look out for ptyalism.

The chief reasons for the superiority of Intramuscular injections of Insoluble preparations of Mercury are their slow absorption, and their gradual and slow elimination. For it is thus that the system is kept under the influence of Mercury for a long time. Mercury administered by the mouth even for prolonged periods, disappears from the urine very soon after the patient ceases to take it. In most cases it has disappeared in less than three weeks from the time its administration ceases: for both absorption and elimination are more rapid when Mercury is given by the mouth, than when injected in the Muscles.

CASES ILLUSTRATING THE RAPIDITY OF ABSORPTION AND ELIMINATION OF MERCURY ADMINISTERED BY THE MOUTH.

CASE. I.

A man took a three grain dose of Pilula Hydrargyri twice daily for three days, from Oct.8th to Oct. 11th. In all he had 18 grains of the pill mass equivalent to six grains of Mercury. A twenty ounce sample of his urine was examined on the 11th and showed definite signs of Mercury, all of which had disappeared in a week.

CASE II.

A man aged twenty-six with secondary Syphilis took two grains of Hydrargyrum cum Cretâ thrice daily, for sixteen days. At the end of

this time I examined a pint of his urine and found he was eliminating Mercury in considerable quantities. In a similar example taken a week later no Mercury could be found.

CASE. III.

A man aged twenty-seven weighing 13st, 4lbs. and of fine physique, had severe secondary Syphilis With Rupia. He had taken four grains of Hydrargyrum cum Cretâ daily for three months, having had in all three hundred and sixty grains, equivalent to one hundred and twenty grains of Metallic Mercury. It had not, however, been sufficient to keep the disease in check, and when first seen by me he had ulceration of both tonsils, mucous patches on the tongue and inner sides of the cheeks, and a very severe secondary rash with rupial sores all over his trunk and limbs. He had also ptyalism, and on examining a pint of his urine on Sep. the 9th. the day I first saw him, I found he was eliminating large quantities of Mercury, about five milligrammes in twenty-four hours. An examination made a week later showed that the amount of Mercury in his urine was reduced almost to vanishing point, and in fourteen days I failed to find any trace of it. He was put on Intramuscular Injections and began to eliminate slowly and regularly, and from the date of the first injection his condition began to improve.

Patients who have been treated by inunction of Mercury, eliminate it more slowly than those who have had it administered by the mouth, but more rapidly than those who have had Grey Oil administered by Intramuscular injections.
In this Country it is almost impossible to get inunction performed with the thoroughness, and penetrative power that can be attained at Aachen, so that any deductions madeastothis point on patients who have been "rubbed" by non-professional rubbers must be accepted with some reserve. But I have examined the urine of two patients after a full course of inunction at Aachen:- equivalent to 120 grammes of the Unguentum Hydrargyri of the German Pharmacopoeia, or to 40 grammes of metallic Mercury, and in neither could any trace of Mercury be found after three months.

The following Table shows the latest date beyond which I have been unable to detect Mercury in the Urine of patients treated by the mouth or by Inunction.

S.	Sex.	Mode of Administration	Preparation of Mercury used	Duration of Treatment	Equivalent in Metallic Hg.	Date of disappearance.
1.	F.	By Mouth	(Liquor Hydrarg (Bichlor	(3drs. daily (for 3 months	12.75 grs.	1 week after last dose.
2.	M.	" Mouth	Hyd. c. Cretâ	(4 grs.daily (for 3 months	120 "	14 days " " "
3.	M.	" Mouth	Hyd.c Cretâ	(6 grs. daily (for 16 days	32 grs	1 week " " "
4.	M.	" Mouth	Liq. Hyd.Bichlor	(3drs. daily (for a monhh	4.2 "	4 days " " "
5.	F.	" Mouth	Pil Hydrarg	(6 grs. daily (for 3 days	6 "	In 1 week" " "
6.	M.	" Mouth	Liq.Hyd.Bichlor	(3 drs. daily (for 4 months	17 "	No Hg. found on 22nd day after ceasing to take it. Precise Date of disappearance unknown.
7.	F.	" Mouth	Hyd. c. Cretâ	(6 grs. daily (for 3 months	184 "	24 days after last dose.
8.	M.	Inunction	Ung.Hydrarg(G.P.)		40 grammes	No. Hg. present after 3 months.
9.	M.	Inunction	" " (G.P.)		40 grammes	No Hg. present after 3 months.

There is no doubt that one of the chief reasons for the extraordinary rapidity with which Mercury disappears from the urine, when it has been administered by the mouth is that it passes unabsorbed through the Intestine.

This is the only feasible explanation of the fact that one may administer Grey Powder over some months in a quantity whose Mercury content is more than one hundred grains, and fail to find traces of it in the urine a fortnight after the administration ceases. Much of it can never have been absorbed, and stored in those known repositories of Mercury in the body, such as the liver. And, as it has not been absorbed, it cannot have exercised its full therapeutic effect. It stimulates intestinal peristalsis both directly through its immediate action, and also indirectly by increasing the flow of bile, which is also an evacuant, and so hastens its own exit from the body.

Mercury injected into the Muscles is eliminated very slowly. When a patient has had a course of twelve injections of seven Centigrammes, it is almost the invariable rule to be able to detect it by Stukowenkoff's method from six to eight weeks later, and in some cases the date of its complete disappearance from the Urine is even more remote.

CASES ILLUSTRATING THE SLOW DISAPPEARANCE FROM THE URINE OF MERCURY INJECTED INTRAMUSCULARLY.

(1)

A Seaman who had had twelve injections, each containing seven centigrammes of Metallic Mercury, the last being administered on August the 31st. reported himself on Nov. 24th. Half-a-pint of his urine was examined, and contained definite traces of Mercury. He had had no Mercury for close on three months.

(2)

A clerk received eighteen injections each containing fourteen Centigrammes of Mercury. The last injection was administered on June 30th and on September 28th Mercury was still being eliminated freely in his urine.

(3)

A male patient received fourteen injections in the course of twelve months, in all receiving one hundred and fifty centigrammes of Mercury. Five weeks after his last injection, six ounces of his Urine were examined and showed a fair quantity of Mercury to be present.

(4)

A midwife who had contracted an extra-genital chancre developed a very severe general infection, which required vigorous treatment. In all she received 14 injections, containing in all 14 grains of Mercury, and in a sample of urine obtained four

months after the last injection, there was still a faint trace of Mercury to be found.

(5)

A Merchant had a course of twelve injections, the first two containing 14 centigrammes of Metallic Mercury, and the other ten containing seven centigrammes each. He received his last injection on Nov. 1st, and on Jan. 9th - almost two and a half months later - Mercury was discoverable in his urine. All these patients were free from kidney disease, so that the slow rate at which they eliminated the Mercury cannot be attributed to any organic defect in their renal organs.

(6)

A Compositor received a single dose of seven centigrammes of Mercury. Three weeks later, he was eliminating it in his urine at the rate of 1 milligramme in each 1000 c.c. of urine voided. No other method of administration known to me, would, with so small a dose, have kept the system so long under the influence of Mercury, and, as will be shown in the chapter dealing with the action of Mercury on the Spirochaeta pallida, this prolonged saturation of the system is of the utmost importance in keeping the micro-organism under control.

I have examined the urine of many patients to ascertain the latest date at which Mercury can be discovered in their urine after a course is completed: and before a patient's second course

of injections has begun I have very often found that Mercury was still being eliminated through the kidneys at the rate of 1 to 2 milligrammes per day. This is not an absolute bar to commencing the second course, but should guide one to choose a smaller dose than usual, and shorten the duration of the second course.

Table: Of cases illustrating the date of Disappearance of Mercury from the Urine after a course Of Intramuscular Injections. In each case the urine was Mercury-free at the time when the course began.

No.	Sex	No. Of Injs.	Amount Of Hg. Injected.	Period Covered by Injections.	Date Of Disappearance From Urine.
1	Male	12	98 cgs.	3 Months	8 Weeks after injections ceased.
2	Male	12	84 "	3 Months	8 Weeks " " "
3	Female	4	28 "	6 Weeks	4 Weeks " " "
4	Male	6	42 "	6 Weeks	5 Weeks " " "
5	Male	6	49 "	6 Weeks	11 Weeks " " "
6	Male	12	105 "	3 Months	15 Weeks " " "
7	Male	10	70 "	3 Months	10 Weeks " " "
8	Female	12	84 "	4 Months	8 Weeks " " "
9	Female	8	56 "	2 Months	6 Weeks " " "
10	Female	6	76 "	6 Weeks	12 Weeks " " "
11	Female	6	42 "	6 Weeks	8 Weeks " " "

No.	Sex.	No. Of Injs.	Amount Of Hg. injected	Period Covered By Injections.	Date Of Disappearance From Urine.
12	Male	3	42 cgs.	3 Weeks	5 Weeks after Injections ceased.
13	Male	12	84 "	3 Months	11 Weeks " " "
14	Male	10	70 "	3 Months	11 Weeks " " "
15	Female	12	84 "	3 Months	13 Weeks " " "
16	Female	8	63 "	3 Months	10 Weeks " " "
17	Female	6	42 "	2 Months	9 Weeks " " "
18	Male	12	84 "	3 Months	12 Weeks " " "
19	Male	10	70 "	3 Months	13 Weeks " " "
20	Male	12	77 "	3 Months	10 Weeks " " "

The relative slowness of elimination of Mercury is therefore obvious. Even so small an amount as 28 centigrammes, or approximately four grains, administered during a period of six weeks, did not disappear from the urine till a month after the last injection. This Table presents a remarkable contrast to the rapid disappearance from the urine of Mercury administered by the mouth.

THE ELIMINATION OF UREA AND CHLORIDES:-

In the course of my analyses of the urine, in dealing with a male patient who was eliminating Mercury slowly, and making but poor progress, it occurred to me to examine his urine quantitatively for urea and chlorides. I found that his excretion of urea and of chlorides was low. As a control I examined the urine of another male patient who had had the same number of injections, and the same amount of Mercury, and who was making rapid improvement, and I found that in the latter case the excretion of urea and of chlorides was very much higher than in the former case. This led me to institute a further series of investigation, and I found that the excretion of chlorides is a very important matter in cases of syphilis treated by Intramuscular injections. In all analyses of this kind, dealing with the salts of the urine, the diet factor is very important, and as all the

patients on whom I have made observations have been out-patients on ordinary diet, there is some room for fallacy in my observations. But as patients with syphilis are not welcomed in the wards of an ordinary Hospital, and as the "Lock" Hospital in Liverpool has now closed all its beds, it has been impossible for me as yet to confirm my results by a systematic examination of the urine of patients on a fixed diet of known chemical composition. But in spite of this fact the results have been so regular and interesting that I am convinced that the urinary chloride excretion of a patient with Syphilis who is receiving Intramuscular injections is not only an indication as to the amount of Mercury he is eliminating by his kidneys, but is also one of the best guides we have as to prognosis.

A patient who, before treatment begins, is eliminating chlorides in the urine in small quantity, will make but slow progress towards recovery, while if his chloride excretion is large, progress is always rapid. The amount of chlorides eliminated in the urine increases as the system passes under the influence of Mercury. A high chloride excretion is usually attended by a free elimination of Mercury in the urine, and so long as the chloride excretion does not fail, one may rest assured that the Mercury is being eliminated well.

A chloride excretion which increases markedly under the influence of Mercury is usually an indication that the patient will make rapid progress, but, as I have convinced myself by experiment, the artificial increase in the chloride excretion of a patient by the administration of Sodium Chloride does not hasten the disappearance of the lesions.

METHODS OF EXAMINATION:-

For the estimation of urea I have employed the usual Hypobromite of Soda method, in Gordon Little's Nitrometer, while for the estimation of the chlorides I have used Mohr's method, which is as follows.

Ten c.c. of urine are diluted in a beaker with 30 to 50 c.c. of distilled water, and treated with a few drops of a 10% solution of Potassium Chromate, till a distinct yellow colouration is produced. A solution of Nitrate of silver containing 29.042 grammes of pure silver nitrate in a litre of distilled water, is then run in from a burette, while the contents of the beaker are kept in vigorous movement. When all the chloride has combined with the silver nitrate and formed a precipitate of silver chloride, any further addition of the silver solution produces a reddish colouration (chromate of silver) which does not disappear on shaking. One c.c. of the silver solution is

equivalent to 0.01 gramme of Sodium Chloride.

As far as possible the samples of urine examined have been typical mixed twenty-four hour samples, but as the work has been done among out-patients it has not always been possible to ensure that the patients have collected and brought their total urinary secretions for 24 hours. However, many of them have systematically done so, and in cases where it has been impossible to secure this, the results of analyses of the urine brought have harmonised closely with the results derived from the examination of the urine of the more attentive patients, and have confirmed my belief in the theories above enunciated. I append herewith a number of Tables illustrating these points.

The Tables have been derived from the systematic examination of the urine of patients who could be relied upon to carefully collect their urine.

Some of the facts tabulated in the succeeding pages are represented graphically in the charts to be found in the Portfolio of Illustrations which accompanies this Thesis. P.p. 24-30.

Mrs.W. age. 45. Old Secondary Syphilis.

Before Treatment Average daily Excretion of urea for a week = 15 grammes.

Before Treatment " " " of Chlorides " a week = 8 grammes.(Calculated as NaCL.)

Date	Injs.	Urea.	Chlorides.	Amount of Hg. in 500 c.c. urine.
1908.				
1.2.	7 cgs.	13.5 grm.	9.grm.	
4.2.		15 "	8.5 "	None recognisable
8.2.	7 "	15. "	4.20 "	" "
12.2.		14. "	9. "	.25 mg.
22.2.	7 "	18. "	12.2 "	.50 mg.
26.2.		16. "	11.5 "	.50 mg.- 75mg.
29.2.	7 "	18. "	11.6 "	.75 mg.
7.3.	7 "	19. "	11.72 "	1 - 1.25 mgs.
10.3.		16. "	12. "	1.25 - 1.50 mg.
14.3.	7 "	14. "	12.6 "	1.50mg.
18.3.		14.5 "	13. "	2 mg.
20.3.		16. "	13.8 "	2 mg.
23.3.		15. "	12.6 "	2 mg.- .25 mg.
25.3.		19. "	13.4 "	2 mg.- .25 mg.

In this case starting from a daily average of 15 grammes of urea, and a daily average Excretion of 8 grammes of Chlorides we find that the wave of urea excretion, but more particularly the wave of chloride elimination rises simultaneously with the increase of Mercury in the urine. Eleven days after the sixth injection the daily excretion of urea was 19 grammes, and the daily excretion of chlorides, calcualted as NaCL was 13.4 grammes. This patient made fairly good progress.

(See Portfolio of Illustrations. P.24.)

Mrs. B. age 34 Primary & Secondary Syphilis.

Average daily excretion of urea before treatment = 11 grammes.
Average daily excretion of Chlorides (as NaCL) before treatment = 6 grammes.

Date	Injs.	Urea	Chlorides	Amount of Hg. in 500 c.c. Urine.
1908				
16.I.	7 cgs.			
17.1.		9.2grms	3.67 grms.	Non recognisable
20.1.		10 grms	5.5 grms	" "
24.1.	7 cgs	12.68 "	7.2 "	" "
28.1.		12.5 "	7.19 "	.25--.50mg.
1.2.		14. "	8.6 "	.25--.50mg.
6.2.	7 cgs	13.6 "	7.84 "	.50 mg.
20.2.	7 cgs	10.8 "	15.6 "	1.50 mg.
24.2.		12.8.	13.2. "	1.75 mg.
2.3.	7 cgs.	9.2	11.22 "	1.75 - 2 mg.
4.3.		16.8	15.	
9.3.	7 cgs	13.6 "	11.5. "	1.75 - 2."
14.3.		16.8.	14. "	2. "
18.3.		14.5.	12.1. "	2.25. "
31.3.		17.3.	15. "	2.25 "
24.3.		13.	15.6 "	2. "
27.3.		15.	18.	

This patient was a poorly developed woman, who obviously had had severe Rachitis in childhood. As will be seen from an examination of the above table her urea elimination, and also her elimination of chlorides were low before treatment with injections began. Both rose under treatment, the urea from 9.2 grammes daily to 15 grammes, and the chlorides from 3.67 grammes (a very low excretion even for her) to 18 grammes. It will be seen that both the urea & the chloride elimination increased as the amount of Hg. in the urine increased.

(See Portfolio of illustrations P.25)

Mr. Halton age 62. Old Tertiary of feet.

Before treatment: Average daily excretion of Urea for a week = 22 grammes.

Before treatment: Average daily excretion of Chlorides for a week = 10 grammes. (Calculated as NaCL.)

Date	Injs.	Urea.	Chlorides	Amount of Hg. in 500 c.c. Urine.
1908.				
14.2.	7 cgs.	13.5 gr.	8.4 gr.	None recognisable.
16.2.		18.2."	8 "	" "
21.2.	7 cgs.	15.8 "	7. "	" "
24.2.		23.4 "	11. "	Microscopic traces.
26.2.		24. "	13.6 "	.25mg
28.2.	7 cgs.	25.2 "	18.4 "	.25 -- .50 mg.
2.3.		27. "	17. "	.50 -- .75 mg.
7.3.	7 cgs.	33.6 "	19.2 "	.75 -- 1 mg.
10.3.		30. "	17.4 "	1 mg.
14.3.	7 cgs.	29.5 "	15.6 "	1.25 mg.
17.		31.gms.	16. "	

The progress made by this patient was very good. The rise in both the chloride and urea waves was marked.

(See Portfolio of Illustrations P.26.)

Mr. H. 31. Old Secondary.

Before treatment: Average excretion of urea daily for a week.= 24 grammes.

Before treatment: average excretion of Chlorides daily as NaCl for a week ==18 grammes.

Date	Injs.	Urea.	Chlorides	Amount of Hg in 500 c.c. Urine.
1908.				
11.2.	7 cgs.	26.4gr.	16 grms.	None recognisable.
14.2.		25.8 "	15 "	" "
20.2.	7 cgs.	25.3 "	18 "	Microscopical traces.
22.2.		26.8."	19.9 "	" "
29.2.	7 cgs.	26.37"	22.50	.25 mg.
3.3.		24 gr"	23.2	.25 --.50mg.
5.3.	7 cgs.	20.32"	21.20	.50 --.75 "
8.3.		24.6 "	23.	.75 -- 1mg.
10.3.	7 cgs.	25.32"	25.20	1 mg.
17.3.	7 cgs.	26. "	22.	1.25 mg.
20.3.		27.	22.4	1.25 mg.

A case in which Metabolism was active, with a high chloride wave, and also a high wave of Urea excretion. This patient did very well.

(See Portfolio of Illustrations P.27.)

F.J. 23. Male. Tertiary Syphilis.

Average amount of Excretion of Urea daily for a week = 16 grammes.

Average amount of Excretion of Chlorides as NaCL. daily for a week. = 14 grammes.

Date	Injs.	Urea.	Chlorides	Amount in Hg. in 500 c.c. urine.
1908				
14.1.	7 cgs.	13	16	
22.1.	7 cgs.	15.4	20.6	(Microscopical
24.1.		18.6	18.	(traces .25 mg.
29.1.	7 cgs.	17.62	23.12	.25 - .50 mg.
2.2.		18.2	16.	.50 mg.
5.2.	7 cgs.	15.61	20.15	.50 - .75
6.2.		19.05	26.60	.75 - 1.mg.
9.2.		18.9	21.5	1 mg 1.25 mg.
14.2.	7 cgs.	17.4.	20.25	1.25 mg.
16.2.		22.	18.4	1.25 mg.
19.2.	7 cgs.	21.2	17.	1.25 - 1.50 mg.
20.2.	7 cgs.	23.1.	22.	1.50 mg.
24.2.		19.8	16.4	1.50 mg.
27.2.		22.6	14.8	1.25 mg.

This patient made good progress. At the beginning of treatment, his chloride excretion was high, and at one period of treatment reached the level of 26.60 grammes of NaCL in 24 hours.

The fluctuations of his Urea Curve of Elimination were not so marked as those of the Chloride Curve, but the general tendency was upward.

(See Portfolio of Illustrations Pg 28.)

W.L. age 30. Tertiary Syphilis. Gummata.

Before treatment: Average daily excretion of Urea for a week = 23 grammes.

Before treatment Average daily excretion of Chlorides for a week. = 12 grammes.(As NaCL.)

Date	Injs.	Urea	Chlorides	Amount of Hg. in 500 c.c. Urine
1907.				
3.12.	14 cgs.	23.6gms.	15.2 gms	None recognisable
7.12.		21. "	17 "	" "
10.12.	14 cgs.	18 "	15.6 "	.25 mg.
14.12.		22 "	14.5 "	.25 -- .50 mg.
17.12.	7 cgs.	29 "	12.8 "	.50 -- .75 mg.
22.12.		28.6"	14.8 "	.75mg.
26.12.	7 cgs.	29.2"	8.4 "	.75 -- 1mg.
30.12		27. "	14.2 "	1 mg.
1908				
3.1.	7 cgs	25. "	15.8 "	1 mg 1.25mg.
5.1.		26.8"	15.6"	1.25mg.
10.1.	7 cgs.	32.	10.5"	1.25mg.1.50
12.1.		31.	12.8"	1.50
16.1.		29.	13. "	1.5mg.

In this case the patient made good progress and the urea and chloride curve rose,as the treatment progressed.

(See Portfolio of Illustrations P.29.)

T.D. Male. age. 37. Tertiary Syphilis.
Before treatment average excretion of Urea daily for a week =25 grammes:
Before treatment Average excretion of Chlorides calculated as NaCl daily for a week = 13 grammes.

Date	Injs.	Urea.	Chlorides	Amount of Hg. in 500 c.c. Urine.
1908				
3.1.	7cgs.	28 grms.	15.4 grms.	None recognisable
7.1.		26 "	15. "	" "
10.1.	7cgs.	25 "	14.8 "	" "
13.1.		26 "	15. "	.25 mg.
17.1.	7cgs.	24 "	16.24 "	.25-.50mg.
21.1.		22 "	16. "	.50-.75mg.
24.1.	7cgs.	33.9"	15.8 "	.50-.75mg.
27.1.		30 "	17. "	.75-1mg.
31.1.	7cgs.	22.5"	18. "	1-1.25mg.
4.2.		24 "	16. "	1.25-1.50mg.
7.2.	7cgs.	27 "	17.5 "	1.50-1.75mg.
10.2.		25 "	15.8 "	2mg.
12.2.		26 "	18.2 "	2mg.25
15.2.		24 "	17.6 "	2mg.
22.2.		22 "	16 "	1.75-2mg.

This patient made very good progress, and an obstinate ulcer over the ankle joint was completely healed after six injections. Before treatment his chloride excretion was high, viz 13 grammes, & during treatment it fluctuated with a generally upward tendency. The highest point in his chloride wave was reached on Feb. 12th when his mercury elimination was also at its height. The fluctuations of his excretions of Urea were not as regular as those of his chloride curve.

(See Portfolio of Illustrations P.30)

M.W. Female. 21. Primary and Secondary Syphilis.

Before treatment: Average excretion of Urea daily for a week = 23 grammes.

Before treatment: Average excretion of Chlorides as NaCL daily for a week = 15 grammes.

Date.	Injc.	Urea	Chlorides	Amount of Hg. in 500 c.c urine.
1908.				
18.1.	7 cgs.	33 grm.	18.7grm.	none recognisable
20.1.	7 cgs	17.6"	20.06"	" "
23.1.		22.4"	19 grm.	.25 mg.
27.1.	7 cgs.	23.6"	19.8 "	.25--.50mg.
28.1.		20.5"	19.9 "	.25--. 5mg.
4.2.	7 cgs.	17.58"	19.6 "	.50mg--.75mg.
7.2.		19.8."	20 "	.75 -- 1 mg.
12.2	7 cgs.	22.5 "	20.08"	1 mg.
15.2.		24.6 "	19. "	1 mg -- 1.25 mg.
19.2.		26. "	21. "	1.25 -- 1.50 mg.
23.2.		26.8 "	18. "	

This case was throughout characterised by a high degree of Chloride Elimination, the average amount eliminated per day being several grammes above normal. The progress made by the patient was excellent. When first seen she had a macular secondary eruption all over the body. It disappeared without going on to the papular stage.

Mrs. Mc. Q. age 25. Secondary Syphilis.
Before treatment: Average Excretion of urine dailyfor a week- 24 grammes.
Before treatment: Average Excretion of Chlorides dailyfor.a week = 10 grammes.(Calculated as NaCl.

Date	Injs.	Urea.	Chlorides	Amount of Hg. in 500 c.c. urine.
1908				
14.1.	14.cgs.	30.7grms.	10.8grms.	
17.1.		20.5	9.	
21.1.	7 "	20.9	9.7	.25mg.
24.1.		15	12.	.25--.50 mg.
28.1.	7 "	17	15	.25--.50 mg.
1.2.		20.2	20.4	.50--.75 mg.
4.2.	7 "	22.	18.	.50mg--.75 mg.
11.2.	7 "	19.2	19.	.75mg--1 mg.
14.2.		23.	14.	.75mg--1 mg.
18.2.	7cgs.	25.5	15.4	1.25 mg-1.50mg.
22.2.		28.	12.	1.25 -- 1.50mg.
25.2.	7cgs.	18.5	11.3	1.50-- 2mg.
27.2.		24.	14.	1.75--2mg.
3.3.		26.	15.4	2mg.
8.3.		25.8	15.	2mg.

In this case starting from a high elimination of urea, the wave of excretion fluctuated considerably. The chloride elimination was throughout very high, and its general tendency was upwards as the system came more under the influence of Mercury.

This patient made excellent progress.

Mr. P. Before Treatment. Average Excretion of Urea daily for a week = 18 grammes

" " " Average excretion of Chlorides daily for a week = 6.5 grammes (As NaCL)

Date.	Injs.	Urea.	Chlorides.	Amount of Hg. in 500c.c.Urine
1908.				
11.1.	7 cgs.	15 grms.	8.32 grms.	None recognisable.
17.1.	7 cgs.	14.8 "	6.8 "	" "
22.1.		18.2 "	7.4 "	" "
25.1.	7 cgs.	23. "	5.22 "	" "
27.1.		20. "	6.8 "	Microscopical traces
1.2.	7 cgs.	9.75"	6.72 "	.25 mg.
4.2.		18.2 "	7. "	.25 mg.
10.1.	7 cgs.	18.2 "	4.57 "	.50 mg.
12.2.		19.4 "	5.8 "	.50 mg.
17.2.	7 cgs.	19.7 "	4.60 "	.50 - .75 mg.
20.2.		18.4 "	6.2 "	.75 mg.
25.2.	7 cgs.	26. "	5.4 "	.75 mg - 1 mg.
27.2.		22. "	7.5 "	1 mg.
5.3.	7 cgs.	27 "	11.6 "	1 mg.
7.3.		20 "	9.8 "	1.25 mg.
10.3.	7 cgs.	20.1 "	10.4 "	1.50 mg.
17.3.		27 "	14.2 "	1.50 mg.

This patient made very slow progress. He was a man of poor physique, and sluggish metabolism. Altogether he had been under treatment for about eighteen months when these observations were made. After the disappearance of his cutaneous symptoms he had syphilitic mischief in the Central nervous system, giving rise to the partial paralysis of the left side. Both his urea and Chloride Excretion were low.

I have systematically examined fifty cases of Syphilis in all stages of the disease, while under treatment with Intramuscular injections, with a view to studying their elimination of Urea and Chlorides, and have arrived at the following conclusions:-

1. Intramuscular injections of Mercury increase the excretion of Urea and Chlorides.

2. The increase of the Chlorides is, as a rule, more marked than that of the Urea.

3. Those patients who have a high Chloride excretion before treatment begins are likely to make rapid progress to recovery.

4. In cases in which the excretion of Chlorides is low before treatment commences the progress of the patient is likely to be slow.

5. Cases which make rapid progress usually show a marked increase in the excretion of Chlorides not later than the week following the second injection.

This I have ventured to designate "The Chloride Response."

6. The increase of the Chloride excretion progresses as a rule pari passu with the increase of Mercury in the urine.

7. So long as the Chlorides are being excreted freely the Mercury will also be excreted freely, and the quantitative test for the Chlorides gives an indication as to whether the Mercury is being eliminated satisfactorily.

8. The Chloride excretion in cases of Syphilis under treatment with Intramuscular Injections of Mercury is a valuable aid in Prognosis.

THE EFFECT OF INTRAMUSCULAR INJECTIONS ON BODY-WEIGHT.

As the treatment promotes Metabolism, it is only natural to find that during a course of injections there will be some increase in the patient's body-weight. This is the almost invariable rule, and my experience has been that during a course of injections patients increase in weight at the rate of from ½ to 3 or 4 ounces weekly. Sometimes after half a dozen injections have been administered the weight begins to fluctuate with a downward tendency. This is an indication to proceed cautiously, and it is a good practice to cease administering any further injections until the weight finds its equilibrium. In cases in which there has been a steady and progressive increase of weight during a long course of injections I have found that a sudden marked decline in weight is the immediate precursor of some symptoms such as diarrhoea or

ptyalism. In my experience with this method of treatment these two occurrences have been very rare, but they have always been preceded by a sudden loss of weight.

CHAPTER

IV.

THE MICRO-ORGANISM OF SYPHILIS.

CHAPTER
IV.

The Micro-organism of Syphilis.

CONTENTS:- Historical:- The Spirochaeta pallida:- Its relation to Syphilis:- Morphological characters Staining properties:- Personal Researches as to frequency in Syphilitic Lesions:- Personal Researches as to absence from non-Syphilitic Lesions:- Personal observations as to Spirochaetae and red blood Corpuscles:- Personal Researches as to action of Mercury on the Spirochaetae:- Life history of the Spirochaeta:- Description of Plates.

---oO@Oo---

HISTORICAL:-

Towards the end of the 15th century Gilinus (6) pointed out that Syphilis is a contagious disease. Some forty years later Massa affirmed that it could be communicated by the linen of a patient with syphilitic sores: but the actual cause was unknown. In the early years of the 16th Century the incidence of the disease was generally ascribed to the wrath of the Creator, or to astral influences, the planets, Saturn and Aries being chiefly incriminated. A humor of the liver, a miasma and the decomposition of semen in the vagina were all regarded, at one time or another,

as causal agents. At this time Syphilis was believed to be transmissible through the air, by food, and by the breath, and Cardinal Wolsey who was affected by it is said (7) to have been arraigned on the charge of whispering into the ear of Henry VIII with a view to communicating the disease to the king. It was not till the middle of the 16th century when Fernel declared that:- "Syphilis is a contagious disease of unknown origin, " and attributed its contagiousness to a virus which he compared to the venom of snakes, that many of the extravagant theories woven around the origin of Syphilis disappeared. This theory of a virus, of an indeterminate nature, has held the field with little successful opposition, ever since.

With the 19th Century came new activities of research. In 1837 Donné described a spirillum which he had found in Syphilitic lesions, and which he called vibrio lineola. Hallier (8) in 1869 stated that he had found in the blood of Syphilitics micrococci which penetrated the red corpuscles, where they developed and produced vacuoles. In 1879 Klebs found in the serum pressed out of a chancre small granulations with rapid movements, and short bacilli, which he was able to cultivate on gelatine, and which, when inoculated into monkeys, set up circumscribed buccal ulcerations, like mucous patches. Shortly afterwards Cutter of Boston claimed to have found a mycelium in indurated chancres.

In 1880, Bermann described Cocci which he found in the lymphatics, and bacteria which he found in the arteries of Syphilitics. In 1881 Aufrecht examined serum from Syphilitic papules and found numerous large cocci often arranged in chains. In 1882 Birsch-- Hirschfeld confirmed Aufrecht's discovery: and the same year Martineau described a Bacterium which he had discovered in an excised chancre. Shortly after Koch announced his discovery of the Tubercle Bacillus, Schutz found, in the serum from chancres, Bacilli which resembled the Tubercle Bacillus. In 1884 Lustgarten (9) observed in gummata and chancres large pale cells in which he described bacilli, difficult to stain and apparently spore-containing. He failed to cultivate and innoculate this organism. In 1885 Babes rediscovered Lustgarten's bacilli, and went so far as to say that their discovery in a doubtful case should confirm the diagnosis of Syphilis. In 1886 Kassowitz and Hochsinger described an organism they had found in the principal organs of five children who had died of congenital Syphilis. From this date practically each year witnessed the announcement of some new organism as the cause of Syphilis. Primo- Ferrari, Doutrelepont, Andronico, von Niessen, and Paulsen were a few only of the discoverers of new Syphilitic organisms, but none of their researches were confirmed by subsequent observers.

In 1901 Justin de Lisle and Louis Jullien (10) found in the blood plasma of untreated cases of syphilis and in blister fluid derived from them, a bacillus of polymorphic character varying from 4-8μ and sometimes seen as an elongated filament. The serum of ~~the~~ Syphilitic patients agglutinated this bacillus, while serum from healthy persons failed to do so. In 1902 Max Joseph and Piorkowski of Berlin described a bacillus for which they claim a specific rôle in the production of Syphilis. But their opinions were not confirmed. In 1905 Siegel, also of Berlin, described an organism, a protozoon, which he had found in Syphilitic lesions, and which he called Cytorrhyctes luis, and it was in prosecuting researches with a view to establishing or disproving the specificity of this organism that Schaudinn and Hoffmann (11) discovered the Spirochaeta pallida. As yet the causal relationship between the spirochaeta pallida and syphilis has not been definitely proved: but the presumptive proofs are very numerous, and continue to accumulate.

PROOFS THAT A MICRO-ORGANISM IS THE CAUSE OF A DISEASE

To establish the causal relationship between any micro-organism and a disease three conditions are necessary:-

1. The organism should be discoverable in all undoubted cases of the disease, either in its

adult form or at some stage of its growth or involution.

2. It should be possible to isolate the organism and secure pure cultures of it.

3. Such pure cultures, inoculated into healthy persons or animals, should produce a disease, or give rise to a train of symptoms resembling, or identical with, the disease or symptoms presented by the person or animal from which the organism was derived.

In the case of some micro-organisms,(e.g. the spirillum of relapsing fever,) generally recognised as the cause of certain diseases, it has not been possible as yet to fulfil all these conditions. And as yet it cannot be said that the spirochaeta pallida has more than a presumptive claim to the title of the causal organism of syphilis. But the evidence in its support is daily becoming stronger. From the time that Schaudinn and Hoffmann (11.12) published their preliminary note in which they announced their discovery of small spirochaetae on the surface of secreting syphilitic eruptions, as well as in the deeper tissues, and in syphilitic inguinal glands, the organisms have been diligently sought for, until to-day one can affirm that the spirochaeta pallida has been found in all the forms, and, practically speaking, all the varieties of syphilitic lesions, and in all the stages of the

disease. When Shennan (13) published his masterly review of the subject, the presence of the organism in tertiary lesions was not generally accepted: and Mc.Weeney (14) had thrown out these suggestions that tertiary and also congenital syphilis might possibly be due to a chronic toxaemia by the metabolic products of the spirochaeta. But evidence is steadily accumulating that the spirochaeta may be found in tertiary lesions, whether deeply situated or superficial. Spitzer (15) has found the organism in several gummata. Dudgeon (16) reports a case in which spirochaetae were found in large numbers in a gumma in a woman with other signs of tertiary syphilis, and Schaudinn himself announced at Lisbon in 1906 that he had found the organism in a gumma of the liver: Badin(17) found undoubted spirochaetae pallidae in tertiary ulcers of the leg, of which he gives an illustration, and also forms less helicoid than usual. Reuter (18) is said to have found the organism in the aortic wall in a case of aortitis.

There are undoubted cases of primary and secondary syphilis in which the most patient investigation has failed to reveal the presence of the spirochaeta: but failure to detect an organism, does not absolutely exclude its presence, so that, to-day, we may say that the first condition necessary to establish a causal relationship between Schaudinn's spirochaeta and syphilis, has been proved.

The second and third conditions must still be regarded as unfulfilled. But Levaditi and MaIntosh,(19) have succeeded in cultivating the Spirochaeta in Collodion sacs placed in the peritoneal cavity of Macacus cynomolgus, and afterwards in rabbits. When subsequently inoculated into monkeys and a Chimpanzee it was found that the Spirochaeta had lost all its pathogenic power. The success obtained by Levaditi and his collaborator, as well as by Tomasczewski, Bertarelli, Hoffman, and Neisser who have grown it on the cornea of rabbits, encourages the belief that shortly the second and third conditions will be satisfied.

MORPHOLOGICAL CHARACTERS:-

The Spirochaeta pallida is a fine thread-like organism, coiled upon itself in its long axis in spiral curves, like a corkscrew. Its curves are short, sharp and regular, excepting at the extremities. The ends are tapering or pointed, and end in flagella. The length of the organism varies from 4 to 14μ. but the average length is about 7μ. or, approximately, the same length as the diameter of a red blood corpuscle. The spirochaeta is extremely narrow, one quarter of a micron being generally regarded as its average breadth. The number of its spirals varies from four to twenty-six though Blaschko has seen a Spirochaeta, which he believed to be the pallida, with only two spirals.

The average number of spirals is between eight and twelve: but my own observations have led me to conclude that the length of the organism and the number of spirals depend largely on the stage of its growth, and its source. Preparations of Spirochaetae, which I have derived from condylomata, have almost always shown organisms of greater length and more numerous spirals than those obtained from the chancre, or secondary papule: and the softer the condyloma, and the more juice could be expressed from it, the more plentiful, the longer, and the more spirally curved have I found the organisms. In a case of extragenital chancre on the scalp, however, I have found longer spirochaetae than I have ever seen from any other source, but this observation is exceptional. In two cases of tertiary Syphilis from which I have succeeded in obtaining what I believe to be specimens of the spirochaeta, the organism did not differ in any essential feature from the organisms found in primary or secondary lesions. The sharp spiral is an essential characteristic of the Spirochaeta, and is present when the organism is moving, at rest, or dried fixed and stained. The organism is very mobile, and its movements are of three kinds (1) A movement of rotation round its longitudinal axis. (2) A movement forward and backward. (3) Movements of flexion of the whole organism.

THE SPIROCHAETA REFRINGENS:-

The Spirochaeta pallida must not be confused with the Spirochaeta refringens which is often found on the surface of chronic ulcers,and also on condylomata and chancres. It is a broader, and usually longer organism than the Spirochaeta pallida, and its curves are blunter, and sinusoidal rather than helicoidal. The ends are blunt, the organism is more highly refractile and stains more deeply than the Spirochaeta pallida. Its role is believed to be a saprophytic one.

THE STAINING OF THE ORGANISM:-

Giemsa's stain which Schaudinn and Hoffmann used in their early experiments, is the one which has given most satisfaction, and though the organism can be stained by many reagents, and even by methylene Blue, Giemsa's combination of Azure and Eosine is undoubtedly the most satisfactory. In my observations I have used Giemsa's stain, and also Bleu-de-Marine which is highly recommended by Levy-Bing. But I have not found the latter stain at all satisfactory for this work.. The drawback to the use of Giemsa's stain is the length of time required. My specimens have all been stained for 20 - 24 hours. The spirochaeta has not an affinity for stains, and consequently does not stain very deeply though the depth of pigmentation may usually be increased by prolonging the time of

immersion in the dye. With Giemsa's stain, the organism stains a delicate shade of red-violet or sometimes a pale rose.

The cilia may be demonstrated if the preparation be first treated with Löffler's mordant, and then stained with Ziehl's Fuchsine. Before his death Schaudinn was able to see the flagella in specimens stained only with Giemsa.

In the tissues the spirochaeta is best seen when stained with Nitrate of silver. For this purpose the method of Levaditi (20) derived from that employed by Ramon y Cajal for the staining of nerve fibrils is generally recognised as the best. As some of the silver remains as a deposit upon the surface of the organism, sections stained in this way show thicker spirochaetae than are to be found in smears, and the specimens of the organism found in such sections should not be used for studying the morphology of the organism. To this must also be added the fact, that, in sections, the organism rarely lies in its whole length in the same plane. It is therefore impossible to focus it all at once and thus see it in its entirety. The best idea of the characters of the organism can be gained by studying it in fresh living preparations, or in stained smears. I have examined thirty-one

cases of syphilis for the spirochaeta. At first, I had no success in finding the organism even from chancres. But, like most other observers, I found that the matter is largely one of habitude, and I have no doubt that if I examined the patients now, in whom I failed to find the spirochaeta at the beginning of my observations, I should be able to demonstrate it. My first four cases, in which I failed to find the organism, may therefore be discounted.

In the following Tables the negative sign — signifies that the Spirochaeta pallida was not found, while the sign X indicates that the organism was discovered.

No.	Sex	Stage Of Disease	Lesions examined	Stain employed	Spirochaetae present?
1	Female	(Primary and (Secondary	Chancre on lip & papules on chest.	Bleu de Marino	---
2	Female	Secondary	Condyloma in Umbilicus	Bleu de Marino	---
3	Female	Secondary	Papules on back	Bleu de Marino	---
4	Male	Secondary	Papules on neck	Giemsa	---
5	Male	Primary	Chancre	Giemsa	X
6	Male	Secondary	Condylomata	Giemsa	X
7	Female	Secondary	Papules on trunk	Giemsa	X
8	Male	Secondary	Papules on back of neck	Giemsa	X
9	Female	Secondary	Papules on labia majora	Giemsa	X
10	Female	Secondary	Condyloma	Giemsa	X
11	Male	Secondary	Mucous patches in mouth	Bleu de Marino	X
12	Male	Secondary	Condyloma	Giemsa	X
13	Male	Secondary	Macules on back	Giemsa	X
14	Female	Secondary	Papules on legs	Giemsa	---

No.	Sex	Stage of Disease	Lesions examined	Stain employed	Spirochaetae present?
15	Female	Secondary	Condyloma	Giemsa	X
16	Male	Primary & Secondary	Chancre & Papules	Giemsa	X
17	Female	Secondary	Rupial sore	Giemsa	X
18	Male	Secondary	Papules & Condylomata	Giemsa	X
19	Male	Secondary	Papules on trunk	Giemsa	X
20	Male	Primary & Secondary	Chancre	Giemsa	X
21	Female	Secondary	Papules on trunk	Giemsa	X
22	Male	Secondary	Papules on trunk	Giemsa	X
23	Male	Primary	Extragenital Chancre on scalp.	Giemsa	X
24	Male	Tertiary	Ulcer of Ankle.	Giemsa	---
25	Female	Tertiary	Ulcer of leg	Giemsa	---
26	Female	Tertiary	Ulcer of leg	Giemsa	---
27	Male	Tertiary	Ulcer of leg	Giemsa	---
28	Female	Tertiary	Ulcer of cheek	Giemsa	---
29	Male	Tertiary	Gumma	Giemsa	---
30	Male	Tertiary	Ulcer of shoulder	Giemsa	X
31	Male	Tertiary	Gumma	Giemsa	X

In addition I have found the Spirochaeta in the liver of a child which died of congenital Syphilis: and I have failed to find it in a case of supposed Syphilis of the lung, and also failed to find it in two placentae from women who had syphilis during gestation. But, as the infants born and the placentae were all free from signs of disease, I did not expect to be successful in discovering the spirochaeta.

As will be seen from the above table twenty-three of the cases examined were in the primary and secondary stages: and in seventeen of these the spirachaeta pallida was present. Eight of the cases showed tertiary manifestations, and in only two of these was I able to find the organism.

In the twenty-three cases twenty-five separate lesions were examined, of which five were primary chancres. As a rule, several smears were taken from each lesion. Of the chancres four yielded a positive result, the only one in which the spirochaeta was not found at repeated examinations being an extragenital chancre on the lip. The lesions included also six condylomata, of which five, all situated in the ano-genital region, showed the presence of plentiful spirochaetae pallidae. One condyloma situated in the umbilicus did not yield any spirochaetae, but as this was one of my early cases, and I did not use Giemsa's stain, I am inclined to attribute my failure to

lack of experience. The other lesions comprised twelve papules with a positive result in eight cases: one macular rash with a positive result: one rupial sore, and one case of mucous patches in the mouth. Both of the latter gave a positive result. Of eight cases of tertiary syphilis examined only two showed any spirochaetae, and in one of these the most careful examination failed to detect more than two organisms in the whole smear. The spirochaeta is therefore difficult to find in tertiary lesions: either because it is scanty in number, which would account for the recognised freedom from contagiousness of the tertiary stage of Syphilis, or possibly in these lesions it occurs in some other form with only an occasional example of the spirochaeta pallida as it is generally recognised. It is well known that the organism of malaria is demonstrable with difficulty in old cases of the disease, and it is generally supposed, that the parasite is therefore few in number: the same is probably true of syphilis. I have examined a number of non-syphilitic cases with a view to ascertaining if the spirochaeta pallida could be discovered in any of them, and invariably with negative results. The procedure followed has been in each case the same as that which I have used in seeking for the spirochaeta in syphilis.
I have made smears from serum obtained from the various lesions, dried them in air, fixed them for ten minutes in absolute alcohol, and stained them for 20-24 hours in Giemsa's solution, and

then examined them with an oil-immersion lens. In one case of balanitis I found the spirochaeta refringens, but in no case did I discover Schaudinn's spirochaeta.

In all I have examined 32 cases as shown in the following table without finding the Spirochaeta pallida in any of them, I have also failed to find it on the healthy genital mucosa both of male and female patients.

In The Following Table the sign --- signifies that the Spirochaeta Pallida was not found.

Disease	Lesions Examined	Site Of Lesion	Result	No. Of Cases Examined.
Eczema	Vesicles	Back Of Hands	---	Five
Psoriasis	Plaques	Back Of Trunk	---	One.
Varicose Ulcers		Legs	---	Ten.
Tuberculosis Cutis	Ulcers	Feet and Arms	---	Three.
Lupus	Nodules	Nose and Face	---	Two.
(Tubercular (Teno-synovitis	Serum from	Round Ankle joint	---	One.
Simple warts		Back Of Hand	---	One.
(Gonorrhœa and (Balanitis	Pus and Serum		---	One.
Balanitis	Pus and Serum	Corona Glandis	(Spirochaeta (Refringens	One.
Epithelioma	Serum	Round Anus	---	One.
Epithelioma	Serum	On Shoulder	---	One.
Abscess	Pus	In Neck	---	One.
Rodent Ulcer	Blood and Serum.	On Face.	---	Four.

THE NUMBER OF ORGANISMS FOUND IN A SMEAR:-

The number of organisms found in a smear varies considerably. Sometimes many fields must be examined before the eye can detect a single example. At other times almost every field has its specimens: and sometimes in one field several spirochaetae may be seen interlaced, or lying close beside each other. From the examination of my specimens I am led to conclude that the smears derived from condylomata are richest in organisms: and this accords with the well know high degree of contagiousness possessed by this type of syphilitic lesion. Smears from chancres come next in their richness in the organism: while small macules and small papules usually contain many fewer spirochaetae.

RELATION OF SPIROCHAETAE & BLOOD CORPUSCLES:-

In preparing smears for the spirochaeta pallida it is well to have as little blood in the film as possible. A smear of pure serum, from a syphilitic lesion, if that can be obtained, usually gives the best results. But if there are any red corpuscles present on the slide it is probable that, in their immediate neighbourhood, one or more specimens of the spirochaeta will be discernable. This fact has been pointed out by other observers, and Mulzer(21)&Ploeger (22) suggest that the red blood corpuscles may carry the parasite through the body. With this theory I do not agree. I believe that the spirochaeta has the power of destroying red blood corpuscles. Anaemia of a varying degree is an early feature of syphilis.

Reiss (23) After examining one hundred cases found that between the appearance of the chancre and the secondary eruption there is a slight decrease in the number of red cells, but the diminution is much more marked after the secondary efflorescence appears. In point of time this diminution, which has been confirmed by Newmann and Konried (24), and which I have myself observed, coincides with the dissemination of the Spirochaeta through the blood stream: and Gaillard (25) found that the red cells increased in number during the first fourteen days of mercurial treatment, which coincides with the period of diminution of the spirochaetae.

In six cases which I have examined during the secondary stage, before mercurial treatment had been instituted, I found the red blood corpuscles much reduced, in one case being as low as 2,736,000 per cubic millimetre, and I found that by the administration of iron the number of corpuscles could be much increased: but, after iron had been administered for a time, I found that if a dose of mercury were administered intramuscularly there was a sudden large increase in the number of erythrocytes. In one of these cases I was able to observe the simultaneous increase in the number of erythrocytes, and the decrease and disappearance of the spirochaetae from the local lesions, and I consider that the parasite can itself-- apart from

its toxins-- destroy the erythrocytes. In smears I have seen red blood corpuscles surrounded and embraced by the spirochaetae (see Portfolio of Illustrations p.36) and I have seen a very large spirochaeta lying close beside a broken up red corpuscle, and I have also seen the extruded nuclei of white corpuscles surrounded by the parasite. To me therefore it seems that the relation between the spirochaeta and the blood cells is not that suggested by Ploeger: but that the spirochaeta is found in the proximity of the red corpuscle with intent to destroy it. For illustrations of these assertions, see portfolio of illustrations p.p.35-37.)

THE ACTION OF MERCURY ON THE SPIROCHAETA PALLIDA.

There is no doubt that it is much easier to find the spirochaeta in a patient who has not had any mercurial treatment, for mercury appears to have the power of greatly lessening the number of spirochaetae, either by its direct influence, or indirectly, by stimulating phagocytosis. Personally, I have never been able to find the spirochaeta in any patient after six injections, of 7 centigrammes of grey oil. Patients in whom the organism was easily demonstrable at the commencement of treatment have been examined over and over again while under the influence of mercury, and I have failed to find the spirochaeta in any of them. But, in spite of this, the spirochaeta has considerable resisting power, even to mercury

applied locally, for I have found numerous spirochaetae in the condylomata of a male patient who had had one intramuscular injection of grey oil, and who had used for five days a dusting-powder containing 33.3 % of Calomel. Unfortunately further observation of this patient was impossible as he went off to sea. I have examined six patients systematically, from the time when treatment began, to ascertain the precise time when the spirochaeta disappeared, with the following results:

No.	Sex.	Stage of Disease.	Lesions examined.	Time when Spirochaetae ceased to be demonstrable.
1.	Female	Secondary	Papules on Trunk	After the 4th injection.of 7 cgs.
2.	Male	Secondary	Papules on back	After the 3rd injection of 7 cgs.
3.	Female	Secondary	Condylomata.	(After six injections of 7 cgs. each. (There was no local treatment in this case.
4.	Male	Secondary	Papules on Trunk	After the second injection.Twoinjections of 14 cgs. each were given at intervals of a week; the spirochaetae were found in "blister fluid" but not after the 2nd. Injection.
5.	Female	Secondary	Papules on Vulva.	The Spirochaetae could not be found after the 3rd injection. The first inj. was of 14 cgs. the two following of 7 cgs. each.
6.	Male	Primary	Chancre on Scalp.	The spirochaeta could not be found after the 2nd inj. The first inj. was of 14 cgs. the 2nd of 7 cgs. The only local treatment consisted in the daily application of boracic compresses.

I have also examined several patients in whose lesions the spirochaetae were easily discoverable before treatment began, at the termination of a course of injections, and in none have I been able to find the organism, either in smears of serum, or in blood-serum obtained from centrifugalised blood. I have also noticed that, as a rule, after the first injection of mercury if it be a full 14 centigramme dose, there is a diminution in the number of spirochaetae demonstrable in a smear either from chancres or secondary lesions, and this diminution progresses, until the system is under the influence of mercury, when the discovery of the organism, except in very rare cases, becomes an impossibility. I do not for a moment suppose that the disappearance of the spirochaeta from the skin lesions of syphilis or even from the blood stream, is to be regarded as an indication that the system is rid of the organism. Experience teaches a very different lesson. But, I believe that, under the influence of mercury, the adult form of the organism - accepting Schaudinn's type as the adult form - is rendered much less plentiful in the system, and the organism enters upon some resting stage, in a form that has not yet been discovered. Schaudinn's type may yet prove to be only one stage in the history of a micro-organism, which has as protean a life -cycle as the malarial

plasmodium. Sooner or later, in most cases, the spirochaeta reappears in its typical aspect, and this is an argument in favour of the "chronic intermittent," treatment with mercury. For, by this method, the system is spared from mercury during the time when the micro-organism. is resting: and when the resting stage is over, and the organisms are mature, they are met by a fresh bath of mercury, which soon destroys them.

The shortest period that I have seen elapse between the termination of a full mercurial course of twelve injections, and the reappearance of the spirochaeta in typical form, is five weeks. A woman, who had a very severe papular syphilis, with rupia, received 12 injections of grey oil. The first two contained 14 centigrammes of mercury each: the other ten contained seven centigrammes each. After the injections I was unable to find any spirochaetae in any of her cutaneous lesions. When her twelve injections were completed, she was in the ninth week of pregnancy. Five weeks after her 12th injection I examined some serum drawn with a Bier's vacuum glass from the remains of a papule on her shoulder. The serum contained a few typical spirochaetae. The mercury in the urine was scanty. From these facts emerge certain principles that should guide us in treatment:-

1. As mercury has the power of causing the disappearance of the spirochaeta it should be administered in efficient doses as soon as the diagnosis of Syphilis is established.

2. As the spirochaeta tends to reappear as the mercury in the system becomes less, the method of administration chosen should be that which keeps the system under its influence for the longest period.

3. The interval between successive mercurial courses should not be too long.

LIFE HISTORY OF THE SPIROCHAETA PALLIDA:-

Krystalowicz and Siedlecki have tried to work out the life history of the spirochaeta pallida, and suggest that at one stage it passes through a trypanosome stage. Their schema is reproduced in photographs J. (Portfolio of illustrations.p 38) where it will be seen that the spirochaeta may divide longtitudinally, or reproduce itself by transverse division. After division they suggest that the organism may either become thicker and more fusiform, losing its sharp spirals, and assuming a trypanosome form (the female type), or may break up into a large number of small pieces,(the male elements)from the conjugation of which the spirochaeta develops again. In this scheme there is still much that requires proof. In my own specimens I have seen many of the forms which Krystalowicz and Siedlecki suggest, but I have failed to find in any specimen the trypanosome-like bodies which they depict. Y-shaped forms as met with in my specimens, I have depicted in plate X Portfolio of illustrations, p.33 and also a spirochaeta showing evidences of thinning in the middle. Fusiform types I have also seen and depicted on plate, X : and the small broken pieces which Krystalowicz and Siedlecki regard as the microgametes, I have also seen and depict at page 33 ,but I have never seen the trypanosome form, and though Schaudinn elaborated a schema to show how Spirochaetae might possibly be developed from trypanosomes,

the trypanosome suggested as playing a part in the life history of the spirochaeta pallida is still a speculation.

There is evidance in favour of an asexual multiplication of the spirochaeta: and by analogy with other protozoa there may be a sexual mode of reproduction. The evidence in favour of the former is the stronger: but the precise method of reproduction in either case is unknown.

DESCRIPTION OF WATER-COLOUR DRAWINGS ILLUSTRATING THIS CHAPTER. See Portfolio of illustrations.p35-38

A. This water-colour drawing is taken from a smear derived from a condyloma. It shows a field rich in spirochaetae pallidae which present the ordinary characteristics of the organism. Types of different lengths are seen, with the sharp helicoidal turns, and the pointed ends. Some are seen to be more or less rectilinear, a type which Fouquet regards as an older form, but the helicoidal spirals are retained even while the organism as a whole is straightened out. Others are seen to be curved into a crescent: while others, especially at the upper part of the picture are interlaced. Towards the lower part of the field is a type frequently met with in which two spirochaetae have a T-like relationship. It has been suggested that this represents a dividing type, but I believe it is due rather to the accidental apposition of two separate organisms.

B. This illustration, which is from a smear from a chancre, shows very well the relationship in which the spirochaetae are very often found to red blood corpuscles. As already indicated, I believe the spirochaetae have the power of destroying the erythrocytes. As will be seen there is considerable poikilocytosis. Though there are spirochaetae in other parts of the field they are grouped specially round the red blood

corpuscles.

C. Water-colour drawing from a smear from a condyloma. In the field is seen a specimen of the spirochaeta refringens, with its wide curves, its thicker body, and its blunt ends. The examples of Spirochaetae pallidae are (a) two of the Y shaped (dividing?)organism. (b) one spirochaeta in the upper part of the field near the Leucocyte, bent on itself like a whip-lash. (c) A very short Spirochaeta with three spirals. (d) A spirochaeta in close proximity to a red blood corpuscle.

D. Drawing from a smear obtained from a chancre, showing the relationship of the spirochaetae to the red blood corpuscles. Near the middle of the field is a distorted corpuscle completely surrounded by interlacing spirochaetae. One of the spirochaetae is definitely inside the eyrthrocyte. It could be brought into view only by focussing more deeply than was necessary to see the spirochaetae on the surface of the corpuscle plainly.

E. Drawing from a smear from an extra-genital chancre on the scalp. A curved spirochaeta is seen close beside a broken red blood corpuscle.

F. Drawing of a smear from a condyloma showing various types of spirochaeta.

Below the red corpuscle is seen a specimen of the spirochaeta refringens. At other parts of the field are seen specimens of the typical form of Spirochaeta pallida, and also other forms thick at one end, and tapering into a long almost invisible, nonrefractile, helicoidal filament.

G. A large epithelial cell from a condyloma showing in its interior, and on its surface, a large number of spirochaetae pallidae. At one part of the cell the organisms are aggregated in a clump: and several are seen not far from the cell nucleus. Fouquet (26) believes that clusters or aggregations of the spirochaeta may occlude blood vessels and give rise to gummata.

H. Smear from an extragenital chancre. Two spirochaetae are seen lying end to end. Longitudinal division?

CHAPTER

V

CLINICAL OBSERVATIONS

CHAPTER

V

Clinical Observations.

CONTENTS:-

Statistics:- Multiple Chancres:- Extragenital Chancres:-
When should Mercurial Treatment begin?-
Types of Syphilitic Lesions:-
Syphilis as an Imitator:-

----oO@Oo----

STATISTICS:- During the past five years I have seen at the Liverpool Skin Hospital, at first as assistant to Dr. Stopford Taylor, and afterwards as full physician, 591 patients suffering from syphilis: of these, 46 were cases of congenital syphilis, and of the remaining 545 cases, 234 were male patients, and 311 female patients. Of the latter 311 female patients no less than 266 were married women or widows, and 200 of the total number of women affected were between the ages of 20 and 40 years - the most fruitful epoch in a woman's life. These figures throw some light on one of the problems of Liverpool life, viz the very high mortality among children under one year of age. In the returns of our Medical Officer of

Health one of the chief causes of these deaths is put down as "Congenital debility;" but the reason of the Congenital debility is not specified. The above statistics suggest that probably many of these deaths are due to inherited syphilis.

In this chapter I propose to give some account of my clinical experiences of the disease, and of the effects of the treatment with intramuscular injections upon it. I shall avoid "text-book" descriptions, and present the types of disease as they presented themselves to me. As a rule patients have first come for treatment when the disease was in the secondary stage, and often we have not seen more than the remains of the primary sore.

MULTIPLE CHANCRES:-

In one case a young man, aged nineteen, presented himself with two definite hard chancres on the penis. Multiple hard chancres in the same patient are not common, but are sometimes met with as in this case. They may develop simultaneously from the same infection, or, a second infection may be acquired at any period within 10 days of the primary infection. After 10 days the body has acquired a certain immunity, and a fresh hard chancre cannot be inoculated. This has been confirmed by Neisser, Wichselmann and Metchnikoff by experiments on anthropoid apes.

EXTRA-GENITAL CHANCRES:-

Among the cases were sixteen of Extra-genital chancres with the following localisations:

(a)	Lip	:	9	Cases:	1	Male:	8	Female:		
(b)	Tonsil:		1	Case :	1	"	"	0	"	:
(c)	Nose	:	1	" :	0	"	:	1	"	:
(d)	Cheek	:	1	" :	1	"	:	0	"	:
(e)	Finger:		3	" :	0	"	:	3	(all midwives)	
(f)	Scalp	:	1	" :	1	"	:	0	"	:
			16							

The situation of the chancre of the lip, was, in each female case, the middle of the mucous border of the upper lip: and in the male case, the right half of the upper lip just below the ala nasi. In the female cases the chancre had been communicated by a kiss: in the male by the cut of a razor.

The chancre on the scalp was due to an injury received in a street fight. The patient "butted" his opponent in the mouth, and sustained a scalp wound which did not heal. When seen, nine weeks afterwards, he had a chancre as depicted (page 39. Portfolio of illustrations.) from which numerous spirochaetae were obtained. He had also a macular secondary rash and general adenitis. The case of chancre on the tonsil occurred in a

glass-cutter age 35, a married man from St Helens. He had also a copious secondary rash, and marked lymphadenitis. The chancre had been inoculated by a "diamond," used in his work. These instruments are served out daily to the men, and no care is taken to ensure that the same instrument is given to the same man each day. When both hands are being employed to break the glass the "diamond," is held in the mouth, and probably a previous user of the tool had had mucous patches in his mouth, from which the contagion had been derived. The tonsil affected was swollen and ulcerated and of cartilaginous hardness. The adjacent retromaxillary lymphatic glands were much enlarged.

The chancre inside the nostril occurred in a woman of 35. How she was inoculated in this situation could not be ascertained. When she was first seen she had a well marked secondary efflorescence.

The chancre on the cheek occurred in a male patient, and the source of infection could not be traced.

The chancres on the finger were all met with in midwives, who, like doctors are particularly exposed to infection in these regions.

(For illustrations of Extra-genital Chancres see Portfolio p. 39)

It has often been asserted that an extra-genital chancre is likely to be followed by a graver systemic infection, than a chancre upon the usual site. All the above sixteen cases ran ordinary courses, and were not more severe than the average case of syphilis with the exception of that of a midwife (see chapter VI) and the man who had a chancre upon the ~~other~~ upper lip. In his case the infection was a very severe one, and he had extensive tertiary ulceration two years after the appearance of the primary sore. I am inclined to think that, if there is any special severity in the ultimate developments which follow an Extra-genital chancre, it is due to inefficient treatment. A person who has innocently contracted an Extra-genital chancre lacks the motive force of shame, and consequently is more likely to be content to undergo treatment only until the immediate symptoms disappear

WHEN SHOULD MERCURIAL TREATMENT BEGIN?

It is still a question much discussed whether antisyphilitic treatment should be commenced on the appearance of the chancre, without waiting for the secondary eruption. As mercury is known to have a definite effect in lessening the virulence of syphilis it is logical to argue that the sooner its administration is begun the better. For, to wait, may be to court disaster: the earliest

secondary symptom proving to be not a cutaneous efflorescence but some lesion in the central nervous system. On the other hand it has been urged that if active mercurial treatment is instituted before the secondary lesions appear they may be inhibited, and a valuable proof is for ever lost that the disease has actually been syphilis. As a result, a patient may be subjected for a long period, unnecessarily, to the influence of a potent and harmful remedy. My opinion is, and it is the practice I have followed, that as soon as a chancre is definitely known to be syphilitic, mercury should be administered. Experience alone can give one the necessary facility in diagnosing the true hard chancre. It is not to be acquired second-hand. Taken together with the clinical history, and the objective appearances, the microscopical examination of a smear from a supposed chancre may yield valuable results. I was recently asked to examine a small erosive papule on the foreskin of a man, which had appeared three weeks after coition. It was very essential that a definite diagnosis should be arrived at immediately, and though I had no doubt from the appearance and character of the papule on palpation, and the history, that the patient had a hard chancre, I made and examined a number of smears stained with Giemsa's solution. I found a large number of spirochaetae in each smear, and recommended that the patient be at once treated with intramuscular injections.

My experience has been that cases in which treatment is instituted early, run a mild course. In the case of a young man who had a definite hard chancre on the fraenum of the prepuce, and who was treated immediately with weekly injections of grey oil, there was never any secondary cutaneous eruption: but between his second and third course of injections he developed some mucous patches in the mouth, which went to prove, though no further proof than his chancre was required, that he actually had syphilis. In cases treated with intramuscular injections before the secondary eruption is in evidence, the severity of the eruption is mitigated, the date of its appearance is postponed and the length of time it is out is shortened: and in such cases I have never seen any tertiary manifestations.

A variable time after the appearance of the chancre - on an average about six weeks - the secondary eruption appears. In the meantime the spirochaeta would appear to be undergoing a second incubation. From the time of infection till the date when the chancre appears - on an average twenty-six days - the spirochaeta is undergoing a first incubation. Thereafter there is a long pause before the secondary efflorescence, and during the interval there are usually such systemic symptoms as lassitude, and headache, with a hard shotty enlargement of the neighbouring lymphatic glands. During this time spirochaetae may be found in the lymphatics running from the primary sore,

the adjacent swollen lymphatic glands, and in very scant number in the blood. (Blaschko)

Just before the appearance of the secondary eruption, there is a sudden, violent systemic invasion by the spirochaetae. I am of opinion that the explanation of the "second incubation period" is that some resisting property of the blood has to be overcome before the organisms can invade the general system: and I suggest that while in the lymphatic glands, where the spirochaetae are known to multiply enormously, they elaborate some toxin, as other micro-organisms do in the course of their growth, which gives rise to the general symptoms. the lassitude and headache etc. and so modifies the blood that the spirochaetae can exist in it.

THE SECONDARY ERUPTION:-

In most cases the secondary eruption of syphilis does not appear till six weeks after the development of the chancre, but this interval may vary from a fortnight which is the shortest period which I have personally observed, to two or even three months, The duration of the secondary stage is generally regarded as being from two to three years. The secondary eruption may be of so slight a nature as to escape altogether the patient's notice or it may be so rebellious as to resist the most energetic treatment, and recur in different forms during several years.

Fournier (27) has seen undoubted secondary syphilis, as long as ten years after the chancre.

The secondary syphilitic eruption is polymorphic: but all its varieties have certain features in common. The chief of the common features are the wide dissemination of the lesions, their superficial character, and their tractability to treatment. As a rule the secondary efflorescence occurs without any febrile disturbance, though I have known of a Chinese patient who had periodical attacks of a feverish nature, accompanied always by an exacerbation of a secondary eruption from which he was suffering. The individual lesions develop slowly, a macular stage usually preceding the completely developed papular stage. The eruption is painless, free from any evidence of local inflammation, and is, as a rule, devoid of any pruriginous sensation. The eruption of syphilis may make its first appearance on any part of the body, though the covered portion- the chest and back - are the regions usually first affected.

TYPES OF SECONDARY ERUPTION:-

The commonest types of secondary syphilitic eruptions among the 591 patients were:-

1. The Roseolar or Macular type, not often seen except as a preliminary to
2. The Papular. Which may be subdivided into
   (a) The small papular.
   (b) The large Papular variety.
3. The ulcerating secondary eruption.(Which is not at all common.)

The macular type is well illustrated by photos 5--4 on page 40 of Portfolio. the former of which shows small macules on the abdominal wall ranged concentrically round the umbilicus, and the latter shows large confluent macules upon the back, some of which are arranged circinately, and have pale centres.

The Macular eruption is of many varieties, but all of them have certain features in common, namely they are never scaly, they are non-pruriginous, and they are slow to disappear. The individual lesion varies in colour. It may be definitely rose-coloured, or, of the generally accepted coppery tint- the hue of a penny that has been in circulation for six months. The lesions are very slightly raised above the surface of the skin, and they can sometimes be felt better by the experienced finger than they can be seen. They do not disappear completely on pressure in all cases.

They may, though very rarely, be arranged in corymbs giving rise to the Corymbose Syphilide, an example of which is well shown in photo p.p.40-41 of Portfolio - a photograph of a young woman of twenty-five. This case was very remarkable in that, though there was no ulceration of the skin during the secondary stage of the disease, the macules, after their disappearance left definite cicatrices, which did not disappear for several months after the subsidence of the efflorescence.

There are all gradations between the macular and the papular syphilitic eruption, and very often the macular stage simply represents a preliminary stage of the papular. In many cases the two types are met with simultaneously as in photo page 41. in which the lesions along and on each side of the vertebral column are definitely papular, while those over the scapulae and over the buttocks are macular. In this case, however, a few days after I took the photograph all the macules had developed into papules. Under the treatment with intramuscular injections I have many times seen a macular eruption completely disappear without becoming papular.

The papular syphilide is the most common variety of secondary eruption, and though it may appear suddenly in a crop scattered all over the body some six weeks after the development of the chancre, it more often develops upon the macule.

The small papular variety, or, as it is sometimes called, the miliary papular syphiloderm, is most plentiful as a rule on the upper part of the trunk, the arms and the thighs. It sometimes affects the face, and I have also seen it on the palms and the soles. The individual lesion is rounded at its base and acuminate. The apex may show a slight depression, the orifice of a follicle, or may be covered by a small vesicle or pustule. The size of the lesion is about that of a lentil, and the colour varies from pale rose to raw-ham.

It may also have a violaceous tinge. Photo p. 41a
After a varying period, according to the severity of the case, and the nature of the treatment, the miliary papular eruption begins to subside. I have seen it persist for months under oral treatment, but, in cases treated by intramuscular injections, I have never seen a case persisting after eight or nine weeks.

THE LARGE FLAT PAPULAR ERUPTION:-

In this eruption the individual lesions may be as small as a split-pea, or as large as a bean. The lesions are generally scattered, the trunk, arms, and upper parts of the thighs being affected. Sometimes also the face shows a copious eruption. Photos p.p. 41a There is little tendency to grouping of the lesions, but sometimes, as a late secondary manifestation which I have seen so long after the primary lesion as seven years, one meets with an aggregation of large papules along the furrow between the nose and the cheek. These often resemble tubercular nodules very closely, especially when they are but slightly elevated. They are of a deep copper colour, and, examined diascopically, are very hard to distinguish from tubercular deposits. Photo page 42
They are very resistent to treatment and I have known one patient who had been treated by many physicians for three years, and had, among other things, had large doses of mercury by the mouth, without any sign of improvement.

On receiving two injections of 14 centigrammes of mercury at intervals of a week a definite improvement was noticed, and after six injections, or in all 84 centigrammes of mercury, the nodules had completely disappeared, leaving no scar. He has been under observation for two years since then, and has had the usual courses of mercurial treatment, and there has been no sign of any recurrence.

THE CIRCINATE SYPHILODERM:-

Another variety of papular syphilide which is sometimes met with, especially as a late secondary manifestation, is the circinate syphiloderm. This is usually met with on the forehead, near the mouth, or on the back of the neck, though I have several times met with it on the back. It consists of a ringed eruption, with a raised and hard border, and a flattened centre, in which, as in the photograph page 42 other circinate elevations may be met with. The peripheral ridge on examination is seen to be composed of a large number of flattened papules, which sometimes show the presence of scales. This is another syphilitic manifestation which is difficult to heal, and often, after its disappearance, its site is marked by pigmentary deposits.

Sometimes the papular syphilide shows a tendency to become squamous, and we get the papulo-squamous syphilide. This type of eruption may be general, but is more often met with as a late and

localised eruption, a "reminder" on palms and soles of the feet. The eruption is modified to some degree in these regions by the thickness of the epidermis, which may be partially detached. There is often a tendency to the confluence of adjacent lesions, which produces the palmar or plantar. serpiginous syphilide(see photos page 43) which is characterised by a loose irregular edge of partially detached and overhanging epidermis which surrounds an exposed and thickened reddish-brown corium. Sometimes there is a tendency as in photo page 43 to fissuring, which can best be overcome by the use of the Unguentum glycerini Plumbi Subacetatis, together with active mercurial treatment. It is somewhat difficult to determine whether this type of lesion should be classed as "secondary". I have seen instances of it occur on the hands and feet in patients who also presented the cicatrices of healed tertiary ulcers on the legs. Perhaps the best name for these lesions is that of Brocq viz Quaternary lesions..

THE CONDYLOMA:- A common form of the papular syphilide is the moist papule or condyloma. It is usually found between contiguous skin surfaces where there are naturally both heat and moisture. Their commonest sites are between the nates, about the genitals in women, and between the scrotum and thighs in man. I have also seen them in the umbilicus,and between the toes.

As a rule they begin as ordinary papules which flatten down through pressure and become macerated by the moisture with which they are bathed. They are reddish-grey, and usually have a thin film of muco-pus on their surface. The French class the mucous patch, so frequently met with in the mouth, with the condyloma under the title of "plaques-muqueuses," (see photo p.44)

RUPIA:- A somewhat rare type of secondary lesion is the Rupial sore, which is a pustular crusted syphilide. It is due to a mixed infection, all the cases which I have examined culturally and microscopically showing the presence of numerous pus organisms. A typical rupia resembles a barnacle stuck in the skin. It is surrounded by a zone of inflammation, and on raising up the crusted mass a purulent discharge oozes from beneath it, and a deep ulcer is exposed. Rupia occurs most often in weakly and dirty patients.

TERTIARY SYPHILIS:-

As potassium Iodide, and not mercury, is generally regarded as the chief remedy for tertiary syphilis, some apology may be needed for introducing into a Thesis dealing with mercury in the treatment of syphilis, any mention of tertiary lesions: but the results I have seen from a combination of intramuscular mercurial injections, and Potassium iodide by the mouth, have been so remarkable that I feel this Thesis would be very incomplete without

some mention of them.

The chief cutaneous manifestations of the tertiary period are the gumma, and the tertiary ulcer.

The gumma is sufficiently well known, and I have nothing to add to its classical description. The general characters of a gumma are well seen in the photo page 44. But among the most remarkable evidences of the efficacy of the intramuscular treatment is the history of the gumma of the tongue shown in photo 21 page 44.

The patient, a woman who smoked, had this gumma in the body of the tongue for one month. The tip and sides of her tongue were cracked and fissured. One intramuscular injection of fourteen centigrammes of mercury was administered and in a week the gumma had completely disappeared. This case illustrates a most important fact regarding the treatment of syphilis affecting the mucous membrane of the mouth. This type of the disease is usually rebellious alike to mercurial treatment administered by the mouth, or by inunction: but yields with remarkable rapidity to intramuscular injections. I have seen several cases of what Fournier calls "Depapillating Glossitis," in which a greater or smaller area of the dorsum linguae had lost its papillae, and presented a smooth, glistening and reddened surface.

In each case the tongue was extremely sensitive, and food, and especially hot drinks caused much pain, Some of these cases had been treated with grey powder or Liquor Hydragyri Perchloridi by the mouth, sometimes for months without improvement, and after one injection of 14 centigrammes of Grey Oil, the patient was conscious of an improvement, and in a week could drink hot tea with comfort. Under the influence of repeated injections the lesion progressed to a complete cure.

Tertiary lesions do not as a rule appear till after two years from the initial infection: but I have seen severe tertiary ulceration appear six months after the chancre.(Photos 23, & 24. P. 45.) This was a severe case of malignant syphilis acquired in Egypt. The patient was a strongly-built man, not intemperate in alcohol, and the virulence of his infection was evidenced by the multiplicity of his tertiary lesions, and the early date of their appearance. He had been treated, with no apparent benefit, on his way from Cairo, with large doses of mercury and potassium iodide by the mouth, and on coming to hospital his case was recognised as of such a severe nature that calomel was administered intramuscularly in one-sixth of a grain doses. After three doses of calomel he was put on full doses

of grey oil, and potassium Iodide, and in three months was completely free from ulceration. The tertiary ulcer is a most formidable lesion. It may destroy the septum of the nose in a week, or eat a hole in the soft palate almost before its presence has been recognised, and, however valuable potassium iodide may be in its control, I am firmly persuaded that the best results by far are to be obtained by combining with the oral administration of potassium iodide energetic intramuscular treatment with grey oil.

A very characteristic form of the tertiary ulcer is the crescentic, or reniform ulcer. The reason for the morphology of syphilitic lesions has not been worked out: but I believe their characteristic shape depends upon the distribution of the finer capillaries. A gumma is circular, because in the first instance it is due to the thrombosis or diminution of the calibre of some small vessel either by clumps of spirochaetae, or by the action of the organism, or its toxins, on the vessel walls: and in a circle of varying radius we get necrotic changes consequent on the cutting off of the blood supply. A tertiary ulcer is crescentic, because a capillary has been occluded at a point where a number of vessels are ramifying from it in one direction.

The tertiary ulcer may occur on any part of the surface of the body: and no internal organ in a syphilitic is free from the possibility of gumma formation. The immediate cause of a tertiary ulcer may be a trauma, in a syphilitic person. Indeed one may assert that any injury occurring to a person with an unexpired syphilitic virus in the system, will give rise to a lesion with definite syphilitic characters.

CASE:-

A woman who had syphilis seven years previously, injured the skin between the thumb and fore-finger with the neck of a broken bottle. There resulted a definitely reniform ulcer, which persisted for eighteen months, but which disappeared completely after the administration of four injections each of seven centigrammes of grey oil, and potassium iodide by the mouth. (phto Pl. 46.)

CASE:-

Even a too strong application of a mercurial ointment will produce a typical tertiary ulcer in a syphilitic patient. I once prescribed dilute nitrate of mercury ointment to a male patient who had had syphilis two years previously for some eczema over the shin-bone. In error he received Unguentum Hydrargyri Nitratis fort. which he applied with vigour, and he returned in four days with two typical tertiary ulcers at the site of inunction.

SYPHILIS AS AN IMITATOR:-

Anyone who has seen much syphilis cannot fail to have recognised its protean character, and must have observed the remarkable way in which it may imitate, with a verisimilitude that almost defies detection, many other cutaneous diseases.

The one syphilitic lesion which does not imitate other lesions is the chancre: but it may itself be imitated more or less closely by the soft chancre, by herpes preputialis, or even by a scabietic pustule.

The secondary rash may imitate, in its roseolar stage, medicinal rashes such as those produced by chloral, copaiba, and cubebs, but the history and the sudden appearance of the latter, together with their brighter red hue, and the adenitis and absence of pruritus in most cases of syphilis should guide one in distinguishing the conditions; and in cases where there is still doubt the subsequent history of the case will clear up the diagnosis.

The small roseolar syphilide may imitate Pityriasis rosea, or Parakeratosis psoriasiforme, but unlike these two diseases it is devoid of scales. It may imitate Seborrhoea corporis as in photos page 47. but Seborrhoea corporis is often attended by pruritus, its lesions are more

definitely fawn-coloured, they present a greasy aspect, show fine scales, and cannot be felt in the texture of the skin, like the roseolar syphilide.

The papular syphilide may imitate acne on the back and chest, but acne in these regions is generally accompanied by a more or less copious eruption, with numerous comedones, on the face: and its elements are of a brighter red colour, and of longer duration than the syphilitic lesions.

Papular syphilis may imitate Lichen planus, but an experienced eye should not have much difficulty in distinguishing between the small flat-topped papule with the glistening surface, and the polygonal outline of Lichen and the rounded papules of syphilis. And, further, most true lichens are intensely pruriginous.

Further, syphilis in its secondary stage may imitate Lupus, and it is often a matter of extreme difficulty to distinguish between the two. In making a differential diagnosis the points to which special attention should be paid are:- (photos 32 & 33. Page 48.)

(a) The history. The duration of a tubercular lesion is likely to be longer than that of a syphilitic one.

(b) The presence or absence of other manifestations of syphilis elsewhere.

(c) The character of the lesions: special attention being paid to the healing centre and the spreading margin of a lupus lesion.

(d) The appearance in Lupus of the deeply seated "apple-jelly" nodule on diascopic examination: though syphilitic nodules may give much the same appearance.

(e) The result of applying Calmette's ophthalmic test with Tuberculin.

I have found this a very sensitive test in known cases of Lupus.

Syphilis in the late secondary stage may give rise to lesions, especially on the scalp, which closely imitate Lupus erythematosus.

In these cases a careful examination should be made for the chacteristic greyish scales with the teat-like processes which characterise the latter disease: and the long duration of the lesion in the latter without extensive destruction should help the diagnosis.

A disease which may be very closely imitated by secondary syphilis is Psoriasis; indeed the condition generally referred to as Psoriasis of the palms or soles is usually syphilitic. The Secondary eruptions may closely resemble Psoriasis, though in the secondary stage the typical sites of election, the back of the elbow joint, and the front of the knee joint, may be spared. In arriving at a diagnosis, the family history, the patient's own previous history, the presence or absence of Psoriasis of the scalp, should help one to a diagnosis.

Sometimes, however, the diagnosis is a matter of extreme difficulty. A postman had a severe psoriatic eruption affecting the back of his hand, his palms, and forearms. There were typical patches at the back of the elbows, and the case appeared, so definitely, psoriasis that no enquiries were made as to a previous infection. He made no progress on the usual treatment for Psoriasis, and on interrogation he admitted having had a chancre seven years previously. He was at once put on intramuscular injections, and in a few weeks the eruption had completely disappeared.

Secondary "reminders" occurring at the typical sites of Psoriasis are often difficult to differentiate. (see photo No.34.p.49.)

This photograph shows a small psoriatic patch over the knee joint of a mid-wife who ten years previously had had an extragenital chancre. The other knee joint, and the elbow joint as well as the scalp and the skin over the sacrum, were free from evidence of Psoriasis, and the lesions quickly disappeared under intramuscular treatment.

Tertiary Syphilis may imitate many conditions e.g. Rodent Ulcer. Here the shorter history of the syphilitic lesions, and, in case of doubt, the result of a microscopical examination should clear the matter up. (Portfolio of Illus. p. 50.)

Tertiary syphilis affecting especially the nose and the upper lip, may closely imitate Lupus. The resemblance is a very marked one if the tertiary manifestation consists partly of ulcerated, and partly of non-ulcerated lesions. A correct diagnosis may be arrived at by considering:-

(a) The duration of the condition - months or years in the case of Lupus and a few weeks or months in the case of syphilis.

(b) The nature of the tissues - which, in the case of Lupus, are soft and friable, in syphilis indurated.

(c) The character of the border of the ulcers which are irregular in the tubercular condition, and regular in the syphilitic.

(d) The effect of Calmette's tuberculin ophthalmo-reaction. (See Portfolio of illustrations p.50.)

CHAPTER

VI.

CLINICAL EXPERIENCES.

CHAPTER.

VI

CONTENTS:-

---oO@Oo---

Any advocate of a special method for the treatment of a disease should be able to adduce proofs that his special Method is efficacious in cases in which other methods of treatment have been tried fruitlessly. In my experience, I have seen many such, but perhaps it will suffice if in this place I give details of four very severe cases of Syphilis that had resisted other energetic forms of treatment, and which yielded rapidly to intramuscular injections of Grey Oil.

CASE. 1. J.R. Male aet 27: He contracted Syphilis in May 1907. and immediately on the appearance of Secondary symptoms was put on

Hydrargyrum cum Cretâ grs. IV daily.

He steadily grew worse, and, although he was a powerfully built man, developed rupial sores on his back, chest. arms and buttocks. When first seen by me in September, 1907 he had a copious maculo-papular rash all over the body, and rupial sores in the regions already indicated. He had circinate eruptions on his face, and pustular Syphilides on his scalp. The tonsils were both ulcerated, as was also the posterior wall of the pharynx. The buccal pouches, and the mucous membrane of the lips showed mucous patches. There were fissuring and cracking of the edges of the tongue, and mucous patches under its body. He had been taking Grey Powder in four grain doses for three months - equivalent to one hundred and twenty grains of Metallic Mercury, and had ptyaliism. That he was absorbing some of the large amount of Mercury he had ingested was obvious from the presence of ptyalism, and from its detection in the urine. He was eliminating between 1 and 2 milligrammes in each 500 c.c. of urine passed. But his disease was progressing from bad to worse.

Although he was suffering from ptyalism, I decided to commence Intramuscular injections as soon as the Mercury disappeared from the urine. I began by a dose of seven centigrammes repeated weekly. After the second dose there was an obvious improvement in the appearance of his cutaneous lesions.

The mucous patches and ulcerations in the mouth and fauces were treated by local applications, and the ptyalism subsided although he was receiving Intramuscular injections. In six weeks the gums were quite firm and free from pain, and after twelve injections, each containing 7 centigrammes of Metallic Mercury, or in all 12.936 grains, the lesions had all disappeared.

Less than thirteen grains of Mercury administered intramuscularly had proved more efficacious in controlling the disease than one hundred and twenty grains of Mercury administered by the mouth.

CASE II. Mrs. R. midwife aet. 54. In the prosecution of her work, this patient contracted a chancre on the finger ten years ago, and was treated by several very capable Liverpool physicians. Her attack was a severe one, and treatment was seriously handicapped by the fact that she tolerated Mercury in any form very badly. Administered by the mouth it set up nausea with loss of appetite, colic and diarrhoea. Administered even in small doses by inunction it provoked a severe dermatitis and colic. Potassium Iodide was no better tolerated and the only remedy which she was able to take, was Sarsaparilla, of whose anti-syphilitic power I have grave doubts. At one time she drank copious

doses of the compound decoction, but there was no improvement in her condition. Ten years after the primary infection she was a broken-down woman, emaciated, her weight being only six stones ten pounds, anemic, and unable to follow her avocation. When first put upon treatment by intramuscular injections she had serpiginous syphilitic lesions on the scalp, the neck the arms and the legs. There were also several gummata on the legs. She received a first injection of 7 cgs. of Mercury on June 14th.1906. and weekly injections of the same size till July, 12th. when a definite improvement was noted. On July the 19th. she volunteered the statement that her appetite was enormous. On November 24th all the cutaneous lesions had disappeared and she said that she had not been so well for years. On Dec. 13th. her first course of treatment finished. In all, she had had 14 injections between June 14th and that date and the actual quantity of Mercury administered was only 14 grains. It was well borne, and did not give rise either to colic or diarrhoea, or any other ill effect. At the end of her treatment she weighed eight and a half stones, and was able to resume her work. In June, 1907. she was in splendid health, and is to-day busily engaged in her work, without any evidence of the disease, from which, for ten years she had been a constant sufferer.

CASE III Mrs. C. aet. 42. She was infected with Syphilis at the age of 33, and developed tertiary ulcers of both legs at the age of 35. At first these ulcers were amenable to treatment, but subsequent ones proved more obstinate. For two years she attended hospital regularly with a large deep reniform ulcer on the back of the left leg just above the ankle, and two ulcers on the dorsum of the same foot. These ulcers were most intractable, and no treatment, either local or constitutional, effected any notable improvement. She had administered to her over long periods the following drugs;-

Liquor Hydrarg Perchlor;-
Potassium Iodide;-
Iodine in the form of the Tincture;-
Donovan's solution, and other varieties of Mercury and the Iodides,

but with no appreciable result. Locally, all manner of dressings were tried, and even the "X"Rays were applied to the ulcers in the hope that they would stimulate repair. She was one of the first patients put on Intramuscular injections when that method of treatment was begun at the hospital, and her improvement was almost immediate. After the second injection of 14 centigrammes of mercury the ulcers began to look healthier, and subsequent injections were reduced to seven centigrammes. After twelve injections, or in all 98 centigrammes i.e. approximately 15 grains of Mercury had been administered, the ulcers had completely healed. During this time no other treatment, except a simple

local dressing, was employed. The ulcers have remained healed, and there has been no recurrence in four years.

CASE 4. E R. Moulder aet. 34. This man contracted Syphilis 7 years ago, and at that time was under treatment with pills for about 18 months. Apparently he got rid of all outward manifestations of the disease, and enjoyed good health till two years ago, when he developed Syphilitic glossitis. He placed himself under the physician who had charge of him during the primary and secondary stages of the disease, and was treated by him with Mercury and Potassium Iodide by the mouth. But the condition proved rebellious, and he steadily grew worse until he was almost unable to eat. Hot drinks of any kind provoked the most acute pain in his tongue: hard morsels of food were intolerable, and he was compelled to live on bread and milk. When I first saw him the whole of the dorsum of his tongue was glazed,and red. Here and there it was actually ulcerated, and there was an almost complete disappearance of papillae. I recognised his condition as that described by Fournier as Depapillating Glossitis, and immediately gave him an injection of 14 cgs. of Mercury. In addition he received a mouth-wash containing acetate of alum. When he reported himself the following week he said

the tongue was less painful, and three days after his second injection, which was of 7 cgs. he was able to drink a cup of hot tea with comfort. He made rapid progess to recovery and after six injections,or in all 49 cgs. of Mercury was able to eat with comfort,an ordinary diet. The tongue, though it had not regained its papillae, had lost its ulcers, and its appearance was much less red and glazed. After 12 injections, though there was still a singular absence of papillae, and the tongue felt very smooth to the touch, he was discharged as cured of his immediate condition. He has since reported himself several times, and when last seen his tongue remained well.

These cases and many others which I might quote, show the superiority of this method of treatment when other methods have failed. And further testimony is afforded by the fact that syphilitic derelicts -- i.e. sufferers from obstinate syphilis, who have drifted from hospital to hospital and tried all remedies without avail - have been amongst the most regular patients to present themselves for their weekly injection. The rapid improvement they make inspires them with fresh hope, and, as in many other diseases, the possession of a new hope is a valuable aid towards recovery.

OBJECTIONS TO THE METHOD:-

The chief critics of the Intramuscular injections are those who have not given them a trial. They argue that the method may be an excellent one for severe and intractable cases, but is too heroic for routine treatment, and should certainly not be used in mild cases. My reply is, that the method is not a heroic one, but simply an effective one, and that by oral medication, one administers a quantity of Mercury far in excess of that given by the Intramuscular method without obtaining so good a result. And as for the contention that the method should not be used in "mild" cases, I would ask "By what criterion can we recognise that a case of Syphilis is a mild one?" The most innocent looking chancre, the most evanes-

-cent secondary rash may be followed by the most formidable tertiary symptoms, either on the surface of the body or in the central nervous system, and it is impossible to say that a man has had a mild attack of Syphilis till he is dead, and his whole life-history can be reviewed. It is a recognised fact that the most severe tertiary lesions are generally met with in patients who have had what has been regarded as a mild infection, and consequently have not been treated with sufficient vigour. Other objections to the method are the alleged dangers of embolism, cellulitis, abscesses, nodes, and the possible injury of important vessels and nerves. In addition, it is said that the Mercury may become encysted in the muscles, and remain unabsorbed for a long period, and then be suddenly absorbed with toxic effects. And the opponents of the method never weary of pointing out that deaths from Mercurial poisoning have followed the treatment.

With these objections I shall deal seriatim.

(1)EMBOLISM:- This can only happen if the Grey Oil is injected directly into a vein. If the injections are properly administered, the needle being inserted first, and an empty syringe being fitted to it and exhausted, one can tell immediately whether a vein has been tapped. If blood is sucked upinto the syringe the needle should be withdrawn

and inserted again at another point. If embolism occurs, it is the fault of the administrator and not of the method.

(2) CELLULITIS AND ABSCESSES.

These conditions are due, not to the Grey Oil but to septic infection. I have not met with either. They do not occur if the patient's skin is well cleaned before each injection, and if the needle and syringe are regularly sterilised, and the Grey Oil kept free from contamination.

(3) NODES:-

These are painful subcutaneous lumps, and never occur if the Mercury is introduced properly into the muscle tissue, and not simply deposited on its surface. In my whole experience I have not met with more than twenty, and the majority of them occurred before I had mastered the technique of the method. In almost every instance in which I have seen them, the patient has been a Woman, and the explanation of their occurrence has been, that there was a large amount of subcutaneous fat between the skin and the gluteal muscle, and the needle was not long enough to pass through the fat into the flesh beyond. Consequently, the Mercury was deposited on the surface of the Muscle, instead of in its substance, and gave rise to a node. A Node generally subsides in a fortnight or three weeks,

and I have never known one to suppurate.

(4) INJURY OF VESSELS AND NERVES:-

The choice of a good site for making the injections, such as that recommended by Barthélemy reduces this risk to a minimum. Of course, if the needle is blindly inserted in the region of the great vessels, or in the line of the sciatic nerve, injury may result, but with a reasonable amount of forethought and care, such an accident should never happen.

(5) STAGNATION OF THE MERCURY IN THE BUTTOCKS, AND SUDDEN ABSORPTION WITH TOXIC EFFECTS:-

This should never occur if the urine is examined from time to time to ascertain whether or not the Mercury is being eliminated satisfactorily. It is neglect of such a simple precaution as this, that has given rise to one of the arguments most frequently directed against the method. I have never known this stagnation occur, and it should certainly never reach dangerous limits if the urine is analysed occasionally, and, if need be, the buttocks examined radioscopically for Mercury. Indeed it is not necessary to make a definite urine analysis for Mercury, for if the excretion of chlorides and urea is satisfactory, the excretion of Mercury, as shown in chapter III will also be satisfactory.

(6) DEATHS FROM MERCURIAL POISONING HAVE BEEN KNOWN TO FOLLOW THE TREATMENT:-

This bogey has been a most powerful deterrent to the general adoption of the method. Very curiously, most of the deaths reported have occurred in France. I was at a loss to understand this till, during a visit to Paris, in May, 1907, I saw more than one hundred injections of Grey Oil administered in the course of one evening at Ricord's old Hospital, by the porter!

If a method that requires skill and precision be delegated to an ignorant attendant, it is natural that disaster should occur. In no case of death, which I have been able to discover in the literature, has there been any systematic examination of the urine for Mercury. In 1901. there were two deaths among our troops in the Egyptian Command. But in neither case is there any evidence that the urine was examined during treatment, for Mercury, nor were the buttocks examined with the "X Rays" on any occasion.

Neglect of such a simple precaution paved the way for this accident.

We do not rule opium out of the Pharmacopoeia because death has followed its administration in too great doses, but we administer it with care. And Grey Oil should not be blamed for disasters attributable solely to its unscientific use.

ADVANTAGES OF THE METHOD:-

The advantages of the method completely outweigh the alleged disadvantages. They are:-

(1)PRECISION OF DOSAGE:-

We know exactly how much Mercury we administer at each dose, and this dose cannot escape from the body without being absorbed.

(2) SMALLNESS OF DOSE:-

In an average case, one grain of Mercury per week is enough to bring about a rapid disappearance of the symptoms. To obtain the same result by oral medication a much larger amount must be administered. In three months a patient will receive twelve grains of Mercury by injection, while in the same period he may take by the mouth over one hundred grains of Mercury, without his disease being controlled.

(3) CERTAINTY OF ADMINISTRATION:-

Anyone, and especially a Hospital patient, is likely to neglect taking his pills or medicine

regularly, and his treatment is interrupted. But in the Intramuscular system the dose is administered by the physician, and the only task laid upon the memory of the patient is the day of the week on which to report himself for his next dose. Three years ago I made statistics as to the regularity of attendance at hospital of fifty patients, who were having Intramuscular injections, and fifty syphilitic patients who had been treated by the mouth before we began the routine practice of injections. I found that, whereas patients treated with mixtures or pills were irregular in their attendance and would for days be without any supply of their remedies, the patients who were receiving injections were exemplary in their regularity, and rarely missed reporting themselves when another injection was due. I have found, too, that the patients return when their second and third courses of treatment are due.

(4)SLOWNESS OF ABSORPTION AND ELIMINATION:-

A priori that form of Mercurial Treatment is most efficient which, for the same dose of Mercury, keeps the system under its influence for the longest time: and in this I believe that the intramuscular injection of Grey Oil is preeminently the best. In chapter II. I have shown the rate at which Mercury is absorbed, and in chapter III. the prolonged period during which it is eliminated, when injected into the buttocks. I have shown that these

processes cover a much longer time than when Mercury is administered by the mouth, and that the Spirochaetae can be discovered again in the lesions as the amount of Mercury in the body diminishes (vide chapter IV.) There is no doubt that the proved superiority of the intramuscular method of administering Mercury is due to the gradual, slow and constant absorption, and the slow elimination of the metal.

(5) PROTECTION OF THE DIGESTIVE APPARATUS:-

Syphilis is, like Phthisis, a disease in which it is necessary to preserve the integrity of the digestive functions. An apparently mild case of Syphilis may assume serious features if, by the administration of remedies by the mouth, the digestion is disturbed, and the patient's vitality is reduced through defective assimilation of his food. Mercury administered intramuscularly reduces this risk to a minimum, and the stomach is left free either for the ingestion of extra nourishment, or the intake of other remedies.

(6)CLEANLINESS OF THE METHOD:-

One great drawback to inunction is its dirtiness, which makes the destruction of all underclothing worn during a "cure" imperative. There is no such disadvantage to the Intramuscular method, which is as clean as it is expeditious.

(7) THE MORAL ELEMENT:-

Many sufferers from Syphilis tend to dwell upon their malady, and thereby become depressed. This depression in some cases amounts almost to melancholia, and it does not promote the patient's recovery to have his disease brought to his mind three or four times daily whenever the hour comes round for his next dose of pills. Injections being administered only once a week, the patient has six clear days in which to forget his malady and the respite thus afforded his nervous system has a valuable tonic effect. I have seen many patients, who have failed to improve with treatment by the mouth, and who were in consequence becoming very depressed, inspired with new hope after the first injection. The novelty of the method, and the idea, rational or not, that Mercury thus injected will find its way into their blood more readily than if taken by the stomach, stimulated their hope, and gave them a fresh hold on life. This quality of a moral tonic is not the least valuable attribute of the intramuscular method.

(8) ITS EFFICACY:-

As already shown, the method is efficacious in cases in which other methods have been tried fruitlessly. I have never known a case which failed to improve under Intramuscular injections, and in some cases, especially those of Glossitis

occurring late in the disease, the method is by far the best available. Its efficacy is the chief argument for making treatment by Injections a routine treatment in all cases of Syphilis.

When we remember the terrible ravages of Syphilis, its immediate effects on the guilty and the innocent, and those serious affections of the circulatory and nervous systems which so often follow in its train, we are compelled to recognise in it one of the most formidable diseases which we have to fight. And in the fight we must, if we hope for victory, use the best weapon at our command which is, I am firmly persuaded, the administration of Metallic Mercury by Intramuscular injections.

CHAPTER

VII

CONCLUSIONS

CHAPTER

VII

CONCLUSIONS

---oO@Oo---

In this chapter I shall do nothing more than gather together a few conclusions at which one may legitimately arrive from a study of the preceding pages.

1. Mercury administered intramuscularly in the form of Grey Oil is absorbed and eliminated slowly. vide Chapters II. and III.

2. In consequence of its slow elimination the system is kept under the influence of Mercury for a long time. Vide Chapter III

3. The total amount of Mercury injected is small, but its full efficacy, exercised over a considerable period, is secured.

4. The Chloride elimination in the urine is a very important factor in prognosis, and is a guide as to the satisfactory elimination of Mercury. Vide. Chapter III

5 The Spirochaeta Pallida is, almost certainly, the causal agent of Syphilis. Vide. Chapter IV.

6. The Spirochaeta Pallida can destroy the red blood cells, and is one of the causes of the Anaemia of Syphilis. Vide. Chap. IV.

7. Under the influence of Mercury the Spirochaeta Pallida disappears from the local lesions of Syphilis. Vide Chapter IV.

8. As the system passes from under the influence of Mercury, the Spirochaeta may again be discovered in the local lesions. Vide. Chapter IV.

9. Consequently Mercury should be administered in intermittent courses, by a method which will keep the system under its influence for the longest time:-i.e. by the Intramuscular method.

10. Clinically, the superiority of Grey Oil in causing a rapid disappearance of the local lesions of Syphilis and in controlling the disease when other remedies have failed is indisputable. Vide. Chapters 5 and 6.

BIBLIOGRAPHY.

---oO@Oo---

1. Wickham:- Practitioner. July 1904.
2. Grosz:- Archiv. f. Dermatologie und Syph. October 1904.
3. Duhot:- Medical Press and Circular Decr.1907.
4. Davidescu:- "Beiträge zum Studium der Ausscheidungswege des Quecksilbers aus dem Organismus "Inaug. Dissert. Bukarest. 1906.
5. Lhereux:- "Du Traitement de la Syphilis par les injections massives." Lyon. 1907.
6. Gilinus:Quoted by Minouflet:-"Etude générale du Treponema Ballidum."Paris. 1906. p.7.
7. Jullien:"Traité pratique des maladies vénériennes." Paris 1879. p.474.
8. Hallier:- Zeitschrift für Parasitologie B- 1.p. 180. 1869.
9. Lustgarten:- Wiener med. Jahrb. 1885. Vol. 1.
10. Justin de Lisle and Louis Jullien:- Journal des maladies cutanées et syph. July 1901.
11. Schaudinn and Hoffmann:- Berliner Klinische Wochenschrift, 1905. p. 22-23.
12. Schaudinn and Hoffmann:- Arbeiten aus dem Kaiserlichen Gesundheitsamts B- 22. Heft 2. April 10th 1905.
13. Shennan:- Lancet:- March 1906.
14. M'Weeney:- British Med. Journal. June 1905.p.1262.

BIBLIOGRAPHY. (Continued.)

15. Spitzer:- Wiener Klin. Wochenschrift Aug. 1905.

16. Dudgeon:- Lancet. March 1906.

17. Badin:- "Recherche du Spirchete Pallida." Bordeaux 1906.

18. Reuter:- Münchener med. Wochenschrift. April 1906 p.778.

19. Levaditi and M-Intosh:- Annales de L'Institut Pasteur. Oct. 1907.

20. Levaditi:-Comptes Rendus. Soc. Biologie. Tome 60. p. 67.1907.

21. Mulzer:- Berliner Klinische Wochenschrift 1905. Sept. 4th.

22. Ploeger:- Münchener Medicinische Wochenschrift 1905.p.1381.

23. Reiss:- Archiv f. Dermatologie u. Syphilis 1895 Heft 1.2.

24. Newmann & Konried:- Wiener Klinische Wochenschrift 1893. No. 19.

25. Gaillard:- Gazette des Hopitaux. 1885. No. 74.

26. Fouquet:- Comptes rendus de la Societe de Biologie 1907. No.5.

27. Fournier:-"Syphilis secondaire tardive". 1906.